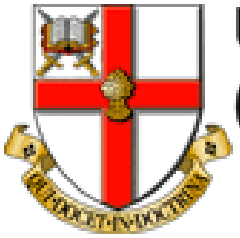

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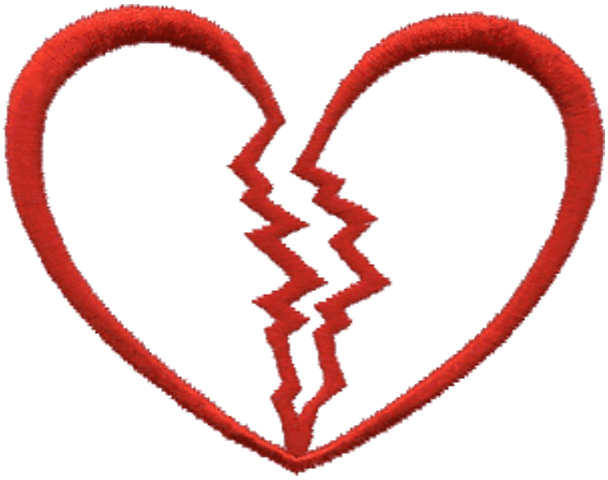
Can cardiac rehabilitation fix a broken heart?

Effect of aerobic exercise on myocardial function in patients with coronary artery disease

A systematic review.



An MSc Thesis by Konstantina Vasileiadi

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Abstract

The benefits of an exercise-based cardiovascular rehabilitation program were well manifested. Psychological aspects of quality of life are important in secondary prevention and quality of life is considerably affected, especially during the initial recovery phase after a cardiac event. A supervised exercise programme should be included in the standard rehabilitation protocol for patients recuperating after myocardial infarction since regularly supervised and prolonged aerobic exercise training improves cardiorespiratory fitness, psychological status, and quality of life and enhances exercise tolerance in patients of all ages, including those older than 75 years and as old as 86 years, who have been excluded from most randomised controlled trials. Modification of lifestyle behaviours such as smoking, eating abundant quantities of fats, sedentary habits, and methods of dealing with stress, can significantly reduce risk of coronary heart disease. Exercise training has a marked effect on the functional status of the patients with acute myocardial infarction and rehabilitation after such an event is aimed at speeding up the patient's return to an active and productive life. Exercise-based programmes have been shown not to only affect physical exercise capacity. They also have implication on every day life by positively affecting the musculoskeletal system, improving osteoporosis, joint flexibility, muscle strength and endurance as well as balance.

Word count: 12,671 words

1. Introduction

Exercise training has emerged as an intervention especially for the secondary prevention of coronary artery disease (Linke, Erbs & Hambrecht, 2006). Aerobic training is an established, inexpensive and generally safe intervention capable of increasing exercise capacity and reducing symptoms in most patients with various cardiovascular diseases (Thompson, 2005). Regular exercise reduces the risk of overall mortality and cardiovascular mortality in particular and exercise is associated with improved activity tolerance, modification of risk factors, such as smoking cessation, hypertension (high blood pressure), dietary patterns, blood cholesterol levels etc., and improvement of quality of life especially in patients with established coronary artery disease (Gassner, Dunn & Piller, 2003).

Despite the growing interest in health promotion, few researchers have seriously, and in depth, examined the remarkable effects of aerobic exercise alone. Cardiovascular societies around the world, such as the European Society of Cardiology (ESC), the American College of Cardiology (ACC), the British Heart Foundation (BHF), the British Cardiovascular Society (BSC) and the Scottish Intercollegiate Guidelines Network (SIGN), nowadays indicate the need for more physical activity than ever. Although, much of this knowledge was compiled during the late 1980s, it has since been revised or discarded on the basis of twenty first century new developments.

Various reports on the state of sedentary individuals warn that inactivity is a major problem and predict an increase in myocardial infarction incidents. Regular exercise training has been conclusively demonstrated to protect individuals from risk of myocardial infarction and sudden death (Squires, 1998) and the type of exercise considered to be particularly beneficial is the dynamic type which is characterized for example by walking, swimming or cycling (Noble, Johnson, Thomas & Bass, 2005). For cardiovascular patients, the results of aerobic exercise training can only be viewed after a long post myocardial infarction period is complete so sometimes it can be difficult to determine how much exercise is sufficient and often uncertainty about the facts leads myocardial infarction patients to more mistakes such as training more than necessary in order to guarantee adequate modification of coronary risk factors.

Cardiac rehabilitation programs developed in the 1960s as a treatment for patients who had sustained a myocardial infarction (Froelicher & Myers, 2006). Before the 1970s, the patient who had a myocardial infarction was almost completely immobilized for six weeks or more and was even washed, shaved, and fed by others in order to keep the work of the heart to a minimum (Froelicher & Myers, 2006). Patients used to maintain activity, including turning over, for several weeks (Cerny & Burton, 2001). Prolonged immobilization not only did not speed healing but exposed the patient to the additional risks of venous thrombosis, pulmonary embolism, muscle atrophy, lung infection and deconditioning (Froelicher & Myers, 2006). Strict bed rest can lead to losses of strength and aerobic capacity approximately 1% to 5% per day and enforced inactivity results in a 15% decrease in stroke volume over several weeks (Cerny & Burton, 2001). Equally serious was the psychological result

of such an approach, which often led to psychological impairment (Froelicher & Myers, 2006).

Rehabilitation of a patient who has experienced a myocardial infarction incident has changed dramatically since the 1960s (Cerny & Burton, 2001). Nowadays, cardiac rehabilitation can be considered as the conservation of human life and its goal is to restore the patient to optimal physiologic, psychological and vocational status (Froelicher & Myers, 2006). Cardiac rehabilitation has become an accepted component of the care plan for patients with coronary artery disease (Squires, 1998). Cardiovascular rehabilitation has been defined as the coordinated sum of different interventions required to ensure the best physical, psychological and social conditions so that patients with chronic or post acute cardiovascular diseases may, by their own efforts, preserve or resume optimal functioning in society and, through improved health behaviours, slow or reverse progression of disease (Fletcher *et al.*, 2001).

More recently, cardiac rehabilitation has been redefined by the Scottish Intercollegiate Guidelines Network and subsequently adopted by the British Association for Cardiac Rehabilitation as the United Kingdom's guideline, as follows: "Cardiac rehabilitation is the process by which patients with cardiac disease, in partnership with a multidisciplinary team of health professionals, are encouraged and supported to achieve and maintain optimal physical and psychosocial health" (Scottish Intercollegiate Guidelines Network [SIGN], 2002). Furthermore, the SIGN guideline acknowledges the key role that exercise plays in contemporary cardiac rehabilitation (Proudfoot, 2006). Cardiac rehabilitation is a comprehensive long term

program which ideally includes, in addition to prescribed, supervised aerobic exercise training, medical evaluation, risk profiling, education and counselling, and coronary risk factor modification by non-pharmacological and pharmacological intervention (Leon, 2000). This includes smoking cessation, hypertension control, blood lipid and lipoprotein management and reduction of excess body weight (U.S. Department of Health and Human Services, 1995 as cited by Leon, 2000).

Cardiac rehabilitation has two aims (Bethell, 2006). First of all, it helps patients to recover as quickly and completely as possible and secondly, it reduces to a minimum the risk of recurrence of the cardiac illness (Bethell, 2006). Cardiac rehabilitation programs now begin within days of an event (Cerny & Burton, 2001). Cardiovascular rehabilitation is now a well, accepted, multidisciplinary health care service that provides patients with a process of developing and maintaining a desirable level of physical, social and psychological well being (Des Jardins, 2002). In addition, rehabilitation now includes patients who have had coronary artery bypass graft artery or coronary artery stent implantation and those who have chronic heart failure (Cerny & Burton, 2001).

The ultimate goal of these rehabilitative services is to help patients with different cardiovascular diseases resume active and productive lives within the limits imposed by their disease process (Leon, 2000). Specific objectives for accomplishing this goal are as follows:

- to limit the physiological and psychological impact of cardiovascular disease
- to optimize functional capacity

- to control cardiovascular and respiratory symptoms
- to reduce the risk of sudden death, reinfarction and even new cardiovascular events
- to prevent the progression or partially reverse the underlying atherosclerotic process
- to enhance the psychosocial and vocational status of selected patients (American College of Cardiology Task Force, 1986 as cited by Leon, 2000).

In the United Kingdom, exercise-based cardiac rehabilitation programs have expanded over the last 40 years and, thanks to funding provided by the British Heart Foundation in the 1980s and 1990s, every hospital in the United Kingdom that treats acute myocardial infarction patients has access to these cardiac rehabilitation programs (Bethell, 2006). The importance of cardiac rehabilitation programs to UK health care was ratified by the National Service Framework for Coronary Heart Disease, which included standards, goals and milestones with the intention that, by 2005, 85% of eligible patients (following acute myocardial infarction or revascularization) should be offered cardiac rehabilitation even though this goal is far from being achieved (Bethell, 2006).

Exercise training indicates exercise performed repetitively to increase the maximal capacity of the oxygen transport (aerobic exercise training) or of the muscular and skeletal (resistance exercise training) system (Thompson, 2005). The terms aerobic and resistance are used to classify exercise despite the recognition that aerobic exercise imposes some load on the muscular and skeletal system and that

resistance exercise also increases oxygen transport (Thompson, 2005). Aerobic exercise training, the cornerstone of a rehabilitation program, can make significant contributions towards achieving each of the below objectives (Leon, 2000) and affords important benefits for most cardiac patients, such as:

- an improvement in exercise capacity and a reduction in symptoms
- less exercise-related ischemia
- improvement in classic coronary risk factors
- improved blood platelet function
- reduced sympathetic nervous system response to mental and physical stress
- decreased psychological disturbance
- a faster emotional resolution after a cardiac event
- a reduction in the rate of progression of coronary atherosclerosis
- lower medical care costs
- improvement in morbidity and mortality for patients with coronary artery disease (Squires, 1998).

General guidelines for exercise rehabilitation programs can be established according to an initial classification of the patient based on the New York Heart Association (NYHA) classification system (Cerny & Burton, 2001) (table 1). Nonetheless, international clinical guidelines consistently identify exercise therapy as a central element of cardiac rehabilitation (SIGN, 2002).

Table 1. New York Heart Association Classification (adapted from the American Heart Association [AHA]).

NYHA Classifications with Expected Exercise Outcomes				
Status	**Characteristics**	**Maximal capacity (METs)**	**Maximal permissible workload (cal/min and METs)**	
I	Can walk without symptoms or limitation; can do most light-effort activities: 0-15% impairment	6.5	Continuous 4.0/3.2	Intermittent 6.0/4.9
II	Has symptoms with light work; slight limitation of physical activity; comfortable at rest; ordinary physical activity results in fatigue, palpitations, dyspnoea or angina:15-30% impairment	>4.5 <6.5	3.0/2.5	4.0/3.2
III	Has symptoms with minimal effort; marked limitation of physical activity; comfortable at rest; les-than-ordinary physical results in fatigue, palpitations, dyspnoea or angina:30-70% impairment	3.0	2.0/1.6	3.0/2.5
IV	Is unable to carry on any physical activity without discomfort; discomfort increases with exercise; symptoms may be present at rest: >70% impairment	1.5	1.0/1.0	2.0/1.6

This review of literature pertaining to exercise training showed that aerobic exercise in post myocardial infarction patients could contribute to the modification of other coronary risk factors, such as blood cholesterol levels, dietary factors and smoking cessation, improve exercise tolerance, reduce all-cause mortality and cardiovascular mortality and enhance quality of life. To better understand how aerobic exercise works in these exercise-based cardiovascular rehabilitation programs, main emphasis of the review was placed on the impact of aerobic training on cardiovascular function and its determinants [cardiac output ($\dot{Q}$), stroke volume (SV), blood pressure (BP), heart rate (HR) and maximal oxygen uptake ($\dot{V}O_2max$)]. Moreover, the changes in exercise parameters such as exercise tolerance, exercise capacity, work tolerance, metabolic equivalents (METs) etc., and in cardiovascular

parameters, such as heart rate, stroke volume, cardiac output, blood pressure, maximum oxygen uptake, double pressure or rate-pressure product, ejection fraction etc., were also reviewed.

This investigation helped to reveal that continuous aerobic exercise training could result in a significant improvement in cardiovascular fitness, especially in groups of cardiovascular patients, and reduce cardiovascular mortality. The results also demonstrated the effects of aerobic exercise, a significant part of the exercise-based cardiac rehabilitation programs and the importance of why all these training components of such programs are so vital to patients with cardiac issues.

2. Aims and objectives

The objectives of this review were twofold. First, the effects of aerobic exercise on myocardial function and more specific on cardiac output ($\dot{Q}$), heart rate (HR), stroke volume (SV), blood pressure (BP) and maximal oxygen consumption ($\dot{V}O_2max$) were examined. Secondly, in which way the alterations of the above cardiovascular parameters are predicted to have an impact in patients with coronary heart disease in a cardiac rehabilitation setting were also investigated.

Questions investigated in this review include:

- What are the effects of aerobic exercise on myocardial function and more specific on cardiac output ($\dot{Q}$), heart rate (HR), stroke volume (SV), blood pressure (BP) and maximum oxygen consumption ($\dot{V}O_2max$)?
- How alterations to myocardial function, as stimulated through aerobic exercise, are predicted to have an impact on patients with coronary artery disease and more specific on patients with myocardial infarction?
- How myocardial function could change as a result of aerobic exercise and how these changes could have a positive effect on patients with coronary artery disease?

The evidence that regular aerobic activity is extremely beneficial in the secondary prevention of coronary artery disease as well as the effects of aerobic exercise training in patients with coronary heart disease were reviewed and last but not least

the benefits of exercise training in coronary heart disease patient groups were examined.

This involved the following specific objectives:

- to examine the effects of aerobic exercise on myocardial function. This involved reviewing data regarding the function of the myocardium and its determinants during aerobic exercise.
- to investigate how these alterations of myocardial function have an impact on patients with myocardial infarction. This involved reviewing data regarding the effects on patients with myocardial infarction.
- to determine how these changes could have a positive effect on patients with coronary artery disease. This involved reviewing data from previous reviews regarding aerobic exercise in exercise based cardiovascular rehabilitation settings.

Thus, the aim was to update the systematic review of the effects of exercise based cardiac rehabilitation in patients with coronary artery disease, and to address previous concerns regarding the applicability of this evidence to routine clinical practice.

3. Methodology

3.1. Search strategy

The research plan proceeded in two phases. During the first phase, a comprehensive literature search of a number of scientific databases, such as Science Direct, Entrez PubMed, ISI Web of Knowledge, Scopus, Medline, the Cochrane Database of Systematic Reviews, the Cochrane Central Register of Controlled Trials and the university library search website was conducted. The Cochrane Library was also searched. The Entrez PubMed related journals facility was concurrently utilized to identify potential investigators within separate journals and to maximize the search for all relevant published articles.

The medical subject headings (MeSH) “aerobic exercise” and “myocardial infarction” and the keywords that were used alone or in combination included “aerobic”, ”training”, ”exercise”, “cardiac”, “rehabilitation”, ”coronary”, ”artery”, “disease”, “heart”, ”myocardial” and “infarction”. Each specific phrase was combined such as “myocardial infarction” AND “exercise training” in order to obtain optimal search capacity within the individual databases (“coronary heart disease and [synonym]” and “rehabilitation or exercise or [synonym]”).

Grey literature was also obtained by searching specialized rehabilitation databases, such as those of the National Rehabilitation Information Center and PEDro

(Physiotherapy Evidence Database). The search engines such as Yahoo and Google Scholar were also used for a variety of materials on the Internet.

The websites of the above databases are:

- Science Direct www.sciencedirect.com
- Entrez PubMed www.ncbi.nlm.nih.gov
- ISI Web of Knowledge www.isiwebofknowledge.com
- Scopus www.info.scopus.com
- Medline http://medline.cos.com
- Cochrane Database of Systematic Reviews www.mrw.interscience.wiley.com/cochrane/cochrane_clsysrev_articles_fs.html
- Cochrane Central Register of Controlled Trials www.mrw.interscience.wiley.com/cochrane/cochrane_clcentral_articles_fs.html
- Cochrane Library www.thecochranelibrary.com
- National Rehabilitation Information Center www.naric.com
- PEDro www.pedro.fhs.usyd.edu.au

The websites for the search engines are:

- Google Scholar www.google.co.uk
- Yahoo www.yahoo.co.uk

Articles were also hand-searched in addition to assessing the above databases in order to maximise the amount of investigations involved in the current systematic literature review. Journals were individually searched for articles that assessed either aerobic exercise alone or aerobic exercise plus counselling or aerobic exercise plus risk factor modification or aerobic exercise plus quality of life which were randomised controlled trials. The journals that were hand-searched as a part of the exploration process were:

- American Heart Journal
- American Journal of Cardiology
- Archives of Internal Medicine
- Archives of Physical Medicine and Rehabilitation
- BMC Cardiovascular Disorders
- British Heart Journal
- Cardiovascular Prevention and Rehabilitation
- Chest
- Circulation
- Coronary Health Care
- European Heart Journal
- Heart
- Journal of the American College of Cardiology (JACC)
- The American Journal of Cardiology
- The Journal of the American Medical Association (JAMA)
- The Lancet
- The New England Journal of Medicine (NEJM)

During the second phase, a more detailed search was conducted on the reference lists from the original research papers. The bibliographies of the retrieved articles were reviewed. So, randomised controlled trials were identified from previously published systematic reviews and meta-analyses. Randomised controlled trials that assigned participants to either an exercise only group or exercise plus counselling or another intervention or a non-training group were potentially eligible to be involved in the current systematic review. All the articles were assessed free electronically through the University of Chester online IBIS Learning Resources facility (http://libcat.chester.ac.uk).

3.2. Selection criteria

Studies were included if

- examined one aspect of cardiac rehabilitation, namely aerobic exercise or aerobic exercise training or exercise training or exercise-based cardiovascular rehabilitation programmes
- were published in English language
- were conducted in humans at least 18 years of age
- randomly assigned patients to intervention and concurrent control groups
- the training program lasted at least two weeks
- must have been added between 1st January, 1990 and 31st July, 2008
- had links to abstracts and full texts.

Reports of randomised controlled trails are the gold standard by which health care professionals and others make decisions about treatment effectiveness (Moher *et al.*, 2001[b]). Most textbooks define the randomised controlled trial as a methodological design that includes random assignment of subjects to two or more subject groups in which the condition or treatment of interest is applied to one of the groups and not to the other (Kane, Wang & Garrard, 2007). Random assignment of subjects is intended to achieve an equalization of subject groups and thereby equally distribute, if not eliminate, extraneous factors that could otherwise influence the study outcomes (Kane, Wang & Garrard, 2007). Moreover, inclusion and exclusion criteria are frequently used to maximize comparability between the treatment and the control groups (Kane, Wang & Garrard, 2007).

The randomised controlled trial is a powerful methodological tool for medical and health care research (Kane, Wang & Garrard, 2007). These randomised controlled trials are the most rigorous way of determining whether a cause-effect relation exists between treatment and outcome and for assessing the cost effectiveness of a treatment (Sibbald & Roland, 1998) and they will and should remain a prominent tool in clinical research (Concato, Shah & Horwitz, 2000). They have several important features:

- random allocation to intervention groups
- patients and trial lists should remain unaware of which treatment was given until the study is completed - although such double blinded studies are not always feasible or even appropriate

- all intervention groups are treated identically except for the experimental treatment group
- patients are normally analysed within the group to which they were allocated, irrespective of whether they experienced the intended intervention (intention to treat analysis)
- the analysis is focused on estimating the size of the difference in predefined outcomes between the intervention groups (Sibbald & Roland, 1998).

Outcomes analyzed in this review included the following: exercise outcomes and more specific, changes on cardiovascular function and its determinants [cardiac output ($\dot{Q}$), stroke volume (SV), blood pressure (BP), heart rate (HR), double product (DP) or rate-pressure product (RPP), ejection fraction (EJ) and maximal oxygen uptake ($\dot{V}O_2max$)], changes in exercise parameters such as exercise tolerance, exercise capacity, work tolerance, metabolic equivalents (METs) etc. Moreover, all cause and cardiac mortality, modifiable cardiac risk factors (blood pressure, smoking cessation and inactivity) and health related quality of life, for example return to work, anxiety or depression were also reviewed.

3.3. Quality assessment

A report of a randomised controlled trial should convey to the reader in a transparent manner, why the study was undertaken and how it was conducted and analysed (Moher *et al.*, 2001[a]). It is the design of choice for evaluating the effectiveness of health care interventions (Huwiller- Müntener *et al*., 2002). To assess the strengths and limitations of randomised controlled trials, readers need and deserve to know

the quality of their methods (Moher *et al.*, 2001[b]). Reporting quality is associated with methodological quality but similar quality of reporting may hide important differences in methodological quality and well conducted trials may be reported badly (Huwiller- Müntener *et al.*, 2002). The assessment of the validity of the primary studies has been identified as one of the most important steps of the peer-review process and as one of the key components of systematic reviews (Jadad *et al.*, 1996).

Previous studies such as the ones conducted by Schultz, Chalmers, Hayes and Altman (1995) and by Moher and colleagues (1999) indicate that reports of low quality randomised controlled trials, compared with reports of higher quality ones, overestimate the effectiveness of interventions by about 30% across a variety of health care conditions. Quality gives us an estimate of the likelihood that the results are a valid estimate of the truth (Moher *et al.*, 1995).

There are three methods to assess the quality of clinical trials: individual markers, checklists and scales (Jadad *et al.*, 1996). Scales and checklists are two types of instruments that may be used to assess the methodological quality of clinical trials (Armijio Olivio *et al.,* 2008). Both scales and checklists include items measuring quality; however, with a scale, the responses to the individual items are summed to create an overall summary score representing trial quality (Armijio Olivio *et al.,* 2008). Scales have the theoretical advantage over the other methods in that they provide quantitative estimates of quality that could be replicated easily and incorporated formally into the peer review process and into systematic reviews (Jadad *et al.*, 1996). The identification of a reliable and valid scale to assess the

literature on a specific topic minimises the chances of errors when determining the quality of the scientific literature (Armijio Olivio *et al.,* 2008).

Numerous scales and checklists have been suggested to evaluate the quality of randomised controlled trials (Moher *et al.*, 1995). However, a five item scale developed by Jadad and colleagues (1996) is the only known scale developed with standard scale development techniques. Although, the scale was developed and validated to assess the quality of reports of pain relief it has been used extensively in other clinical areas as it is quite efficient to use (Clark *et al.*, 1999). The Jadad scale has also been adapted for use in many health care areas such as medicine, dentistry, psychology and physical therapy (Armijio Olivio *et al.,* 2008). In addition, the Jadad scale is by far the most commonly used scale by the health care community (Armijio Olivio *et al.,* 2008). The items on the Jadad scale are presented as questions to elicit a “yes” or “no” answer (Jadad *et al.*, 1996) composed of the following instructions:

It should not take more that ten minutes to score a report and there are no right or wrong answers (Jadad *et al.*, 1996). Please read the article and try to answer the following questions (Jadad *et al.*, 1996):

- Was the study described as randomised (this includes the use of the words such as randomly, random and randomization)?
- Was the study described as double blind?
- Was there a description of withdrawals and dropouts?
- Was the randomization described as appropriate?

- Was the blindness described as appropriate? (Jadad *et al.*, 1996).

Scoring the items:

Either give a score of one point for each “yes” or zero points for each “no and there are no in-between marks (Jadad *et al.*, 1996).

Give one additional point if :	For question one, the method to generate the sequence of randomization was described and it was appropriate (table of random numbers, computer generated etc.) (Jadad *et al.*, 1996).
and/or :	For question two, the method of double blinding was described and it was appropriate (identical placebo, active placebo, dummy etc.) (Jadad *et al.*, 1996).
Deduct one point if:	For question one, the method to generate the sequence of randomization was described and it was inappropriate (patients were allocated alternately, according to date of birth, hospital number etc.) (Jadad *et al.*, 1996).
and/or :	For question two, the study was described as double blind but the method of blinding was inappropriate (e.g. comparison of tables vs. injection with no double dummy) (Jadad *et al.*, 1996).

Guidelines for assessment:

1. Randomization

A method to generate the sequence of randomization will be regarded as appropriate if it allowed each study participant to have the same chance of receiving each intervention and the investigators could not predict which treatment was next

(Jadad *et al.*, 1996). Methods of allocation using date of birth, date of admission, hospital numbers or alternation should not be regarded as appropriate (Jadad *et al.*, 1996).

2. Double blinding

A study must be regarded as double blind if the word “double blind” is used (Jadad *et al.*, 1996). The method will be regarded as appropriate if it is stated that neither the person doing the assessments nor the study participant could identify the intervention being assessed, of if in the absence of such a statement the use of active placebos, identical placebos or dummies is mentioned (Jadad *et al.*, 1996).

3. Withdrawals and dropouts

Participants who were included in the study but did not complete the observation period or who were not included in the analysis must be described (Jadad *et al.*, 1996). The number and the reasons for withdrawal in each group must be stated. If there were no withdrawals, it should be stated in the article (Jadad *et al.*, 1996).If there is no statement on withdrawals, this item must be given no points (Jadad *et al.*, 1996).

The Jadad scale focuses only on randomization, blinding and withdrawal and dropouts in order to evaluate methodological quality of primary research (Armijio Olivio *et al.,* 2008). It contains a total of three questions, two concerning randomisation and the blinding of the study with an additional question assessing the reported dropouts and withdrawals (Jadad *et al.*, 1996). Each criterion is awarded with a point if it can be answered adequately, although if the reply to the third

question is negative then a point is deducted (Jadad *et al.*, 1996). A simple calculation is then performed to derive a total and scores of three, or even above, out of five are usually accepted as indicative of high quality randomised controlled trials (Jadad *et al.*, 1996). When using the Jadad scale, it may be important to ensure that good agreement is achieved prior to using the scale (Clark *et al.*, 1999) since a major disadvantage of the instrument described above is that the assessment of the quality of a randomised controlled trial depends on the information available in the reports (Jadad *et al.*, 1996) (figure 1).

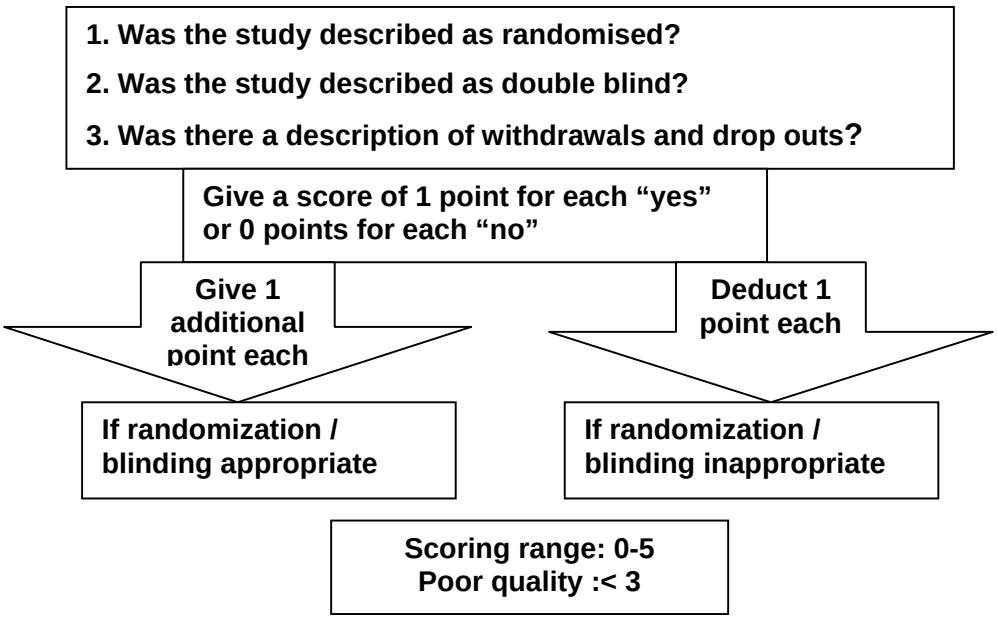

Figure 1. Validated quality scale (adapted from Jadad, A.R. *et al*. (1996) Assessing the quality of reports on randomised clinical trials: Is blinding necessary? *Controlled Clinical Trials*, 17, 1-12).

One limitation surrounding this tool is the simplicity of the scale, as it doesn't explore an investigation's methodology which if reported poorly can have consequences on the results used within a systematic review or a meta-analysis. Moreover, the validity of the results is threatened by the subversion of randomization, resulting in biased allocation to comparison groups, the unequal provision of care apart from the intervention under evaluation, the biased assessment of outcomes and the inadequate handling of dropouts and losses to follow-up (Huwiler-Müntener *et al.*, 2002). Therefore, the Jadad scale may be a quick and effective tool which can be used to incorporate studies into a systematic literature review such as this:

Study	**Lee et al.(2008)**
1) Was the study described as randomised?	1
2) Was the study described as double blind?	0
3) Was there a description of withdrawals and dropouts?	1
4) Was the randomization described as appropriate?	1
5) Was the blindness described as appropriate?	0
Total Jadad score	3/5

Therefore, the above article is considered as a consistent high quality randomised controlled trial because it is within the three to five point range on the Jadad scale (Jadad *et al.*, 1996).

Non pharmacologic trials usually test complex interventions involving several components (Boutron *et al.*, 2008). Such treatments are consequently difficult to describe, standardize, reproduce and administer consistently to all patients (Boutron *et al.*, 2008). Non pharmacologic treatments cover a wide range of interventions including surgery, technical procedures (for example angioplasty), implanted devices (for example pacemakers), non implantable devices, rehabilitation, physiotherapy, behavioural therapy, psychotherapy and complementary and alternative medicine (Boutron *et al.*, 2008). To help improve the quality of reporting such randomised controlled trials, the Consolidated Standards of Reporting Trials Group developed the CONSORT statement (Begg *et al.*, 1996), which is a 22-item checklist and flow diagram (Moher *et al.*, 2001[a]).

The CONSORT Statement published in 1996 and revised in 2001 is a set of guidelines designed to improve the reporting of randomised controlled trials (Altman *et al.*, 2001) and an evidence based approach to help improve the quality of reports of these trials (Moher *et al.*, 2001[b]). The CONSORT statement (or simply CONSORT) comprises of a checklist of essential items that should be included in reports of randomised controlled trials and also a diagram for documenting the flow of participants through a trial (Altman *et al.*, 2001). The objective of CONSORT is to facilitate critical appraisal and interpretation of randomised controlled trials by providing guidance to authors about how to improve the reporting of these trials (Altman *et al.*, 2001).

Since its publication in 1996, the CONSORT statement has been widely supported (Altman, 1996), has been translated into several languages and even has an Internet

presence (www.consort-statement.org/) in order to facilitate awareness and dissemination (Moher *et al.*, 2001[b]). The CONSORT checklist provides a method of standardising the way which items are reported, making the experimental process more transparent within trials (Moher *et al.*, 2001[b]). The checklist and the flow chart are primarily intended for use in writing, reviewing or evaluating reports of simple two-group parallel randomised controlled trials (Moher *et al.*, 2001[a]). It has been endorsed by the World Association of Medical Editors (WAME, www.wame.org) , the International Committee of Medical Journal Editors (ICMJE, www.icmje.org), the Council of Science Editors(CSE, www.counsilscienceeditoris.org) and over 200 journals worldwide (www.consort-statement.org/index.aspx?o=1096). The CONSORT checklist is intended to improve the reporting of a randomised controlled trial, enabling readers to understand its conduct and to gauge the validity of its results (Plint *et al.*, 2006).

Journal adoption of the CONSORT checklist is defined as a statement in the "instructions to authors" section in order to follow the CONSORT statement in preparing manuscripts or a requirement for authors to submit a completed CONSORT checklist with their manuscript (Plint *et al.*, 2006). In 2001, Moher and colleagues determined whether the use of the CONSORT statement was associated with improvement in the quality of reports of randomised controlled trials. They suggested that the use of CONSORT checklist may be associated with improving the quality of reports of randomised controlled trials (Moher *et al.*, 2001[b]). Higher quality reports are likely to improve randomised controlled trial interpretation, minimise biased conclusions and ultimately facilitate decision making about treatment effectiveness (Moher *et al.*, 2001[b]).

In 2005, Altman conducted a study of journal endorsement of the CONSORT Statement and found that nine years following its initial publication, and four years after its update, only 22% of the 166 high impact factor journals provided any mention of CONSORT statement in their published section “Instructions to Authors” and 25% of these referred to the obsolete 1996 version (Altman, 2005). In another study, involving 15 high impact journals (five of which were not included in the previously mentioned review by Altman, 2005) that have reported endorsing the CONSORT statement, only eight referred to the statement in their instructions to authors section (Mills *et al.*, 2005[a]). In a study of randomised controlled trials in journals that adopted the original CONSORT statement and then the revised version, the authors found that the quality of reporting of blinding improved by 23% to 55% between publication of the two checklists (Mills *et al.*, 2005[b]).

The CONSORT checklist of 22 questions evaluates items that are vital for a randomised control trial to be adequately detailed (Mills *et al.*, 2005[a]).Numerous investigations have examined the use of the CONSORT checklist to maintain the high standards associated with randomised controlled trial methodological designs (Moher *et al.*, 2001[b], Kane, Wang & Garrard, 2007). The rationale for utilizing the CONSORT is that this methodology evaluates a number of factors used to represent a well performed randomised controlled trial (Moher *et al.*, 2001[b]). However, the CONSORT checklist has been employed in a greater number of high impact general medical journals than more specialised medical journals (Mills *et al.*, 2005[a]). Moreover, Plint et al. (2006) identified that the CONSORT checklist may be a successful tool to critically appraise studies within a systematic review. Quite recently, Hopewell and colleagues (2008) examined the online version of

"Instructions to Authors" for 165 high impact factor medical journals and extracted all text mentioning the CONSORT Statement or CONSORT extension papers. There was a relative increase of 73% from the survey by Altman (2005) (Hopewell *et al.*, 2008).

CONSORT Statement (adapted from Begg *et al.*, 1996)

PAPER SECTION And topic	Item	Descriptor	Reported on Page #
TITLE & ABSTRACT	1	How participants were allocated to interventions (e.g., "random allocation", "randomised", or "randomly assigned").	
INTRODUCTION Background	2	Scientific background and explanation of rationale.	
METHODS Participants	3	Eligibility criteria for participants and the settings and locations where the data were collected.	
Interventions	4	Precise details of the interventions intended for each group and how and when they were actually administered.	
Objectives	5	Specific objectives and hypotheses.	
Outcomes	6	Clearly defined primary and secondary outcome measures and, when applicable, any methods used to enhance the quality of measurements (e.g., multiple observations, training of assessors).	
Sample size	7	How sample size was determined and, when applicable, explanation of any interim analyses and stopping rules.	
Randomization -- Sequence generation	8	Method used to generate the random allocation sequence, including details of any restrictions (e.g., blocking, stratification)	
Randomization -- Allocation concealment	9	Method used to implement the random allocation sequence (e.g., numbered containers or central telephone), clarifying whether the sequence was concealed until interventions were assigned.	
Randomization -- Implementation	10	Who generated the allocation sequence, who enrolled participants, and who assigned participants to their groups.	
Blinding (masking)	11	Whether or not participants, those administering the interventions, and those assessing the outcomes were blinded to group assignment. If done, how the success of blinding was evaluated.	

Statistical methods	12	Statistical methods used to compare groups for primary outcome(s); Methods for additional analyses, such as subgroup analyses and adjusted analyses.	
RESULTS Participant flow	13	Flow of participants through each stage (a diagram is strongly recommended). Specifically, for each group report the numbers of participants randomly assigned, receiving intended treatment, completing the study protocol, and analyzed for the primary outcome. Describe protocol deviations from study as planned, together with reasons.	
Recruitment	14	Dates defining the periods of recruitment and follow-up.	
Baseline data	15	Baseline demographic and clinical characteristics of each group.	
Numbers analyzed	16	Number of participants (denominator) in each group included in each analysis and whether the analysis was by "intention-to-treat". State the results in absolute numbers when feasible (e.g., 10/20, not 50%).	
Outcomes and estimation	17	For each primary and secondary outcome, a summary of results for each group, and the estimated effect size and its precision (e.g., 95% confidence interval).	
Ancillary analyses	18	Address multiplicity by reporting any other analyses performed, including subgroup analyses and adjusted analyses, indicating those pre-specified and those exploratory.	
Adverse events	19	All important adverse events or side effects in each intervention group.	
DISCUSSION Interpretation	20	Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision and the dangers associated with multiplicity of analyses and outcomes.	
Generalizability	21	Generalizability (external validity) of the trial findings.	
Overall evidence	22	General interpretation of the results in the context of current evidence.	

CONSORT Statement

Lee et al. (2008)

PAPER SECTION **And topic**	**Item**	**Descriptor**	**Reported on Page #**
TITLE & ABSTRACT	1	How participants were allocated to interventions (*e.g.*, "random allocation", "randomised", or "randomly assigned").	Post-infarction patients were randomly assigned to a training group or a nontraining group.
INTRODUCTION Background	2	Scientific background and explanation of rationale.	Cardiac rehabilitation is believed to increase myocardial perfusion reserve (MPR) but this has not been adequately studied because of poor delineation of infarcted myocardium in previous studies. The purpose of this study was to determine the effect of cardiac rehabilitation on myocardial perfusion reserve with contrast-enhanced magnetic resonance imaging.
METHODS Participants	3	Eligibility criteria for participants and the settings and locations where the data were collected.	Men aged ≤65 years old with a history of myocardial infarction for at least 3months before screening were eligible. The inclusion criteria were a successful procedural outcome after primary stenting during the initial myocardial infarction treatment, a clinically stable course for at least 3 months after discharge and no evidence of myocardial ischemia on initial and follow-up exercise testing. This study was performed at the National Taiwan University Hospital.
Interventions	4	Precise details of the interventions intended for each group and how and when they were actually	At the baseline and 3-month follow-up assessment, all patients underwent a

		administered.	functional evaluation, which included clinical evaluation, exercise testing and cardiac magnetic resonance imaging.
Objectives	5	Specific objectives and hypotheses.	The primary aim of the present study was to investigate whether cardiac rehabilitation influences perfusion differently in the infarcted and remote myocardium. The secondary aim was to assess the relation between myocardial perfusion reserve and exercise capacity.
Outcomes	6	Clearly defined primary and secondary outcome measures	Cardiac magnetic resonance imaging is an excellent diagnostic tool for serial assessment of changes in left ventricular structure and function, infarct location and size, and myocardial perfusion reserve. The ability of cardiac magnetic resonance imaging to assess concurrently and with high spatial resolution the extent of scar tissue in the myocardium and perfusion is one of the major strengths of this technique.
Sample size	7	How sample size was determined and, when applicable, explanation of any interim analyses and stopping rules.	39 patients were enrolled. After completing the initial evaluation, they were randomly assigned to the 3-month training program (n=20) or the non-training group (n=19). For comparison of exercise capacity and myocardial perfusion, 19 age-, weight-, and height-matched subjects without cardiovascular risk factors were selected as healthy controls.
Randomization --	8	Method used to generate the random allocation	Random assignment with no more details

Sequence generation		sequence, including details of any restrictions (*e.g.*, blocking, stratification)	was used to allocate participants to either training or no training group.
Randomization -- Allocation concealment	9	Method used to implement the random allocation sequence (*e.g.*, numbered containers or central telephone), clarifying whether the sequence was concealed until interventions were assigned.	---
Randomization -- Implementation	10	Who generated the allocation sequence, who enrolled participants, and who assigned participants to their groups.	Allocation, sequence and enrolment were performed by the authors involved in the present investigation.
Blinding (masking)	11	Whether or not participants, those administering the interventions, and those assessing the outcomes were blinded to group assignment. If done, how the success of blinding was evaluated.	No information regarding blinding was mentioned
Statistical methods	12	Statistical methods used to compare groups for primary outcome(s); Methods for additional analyses, such as subgroup analyses and adjusted analyses.	Calculations of statistical power for the primary end point of the peak VO_2 based on previous data in post- myocardial infarction patients showed that a power of 0.8 was needed to detect a 14% increase at a 5%significance level with a minimum. Of 17 subjects per group. All data are presented as the mean± standard deviation for continuous data and as proportions of binary data. If the data were not distributed normally, natural logarithmic transformation was used for analysis. Correlations were tested using Pearson analysis. Baseline characteristics were compared using the unpaired Student's *t* test for continuous data and chi-square analysis for binary data. Changes in data from the baseline to follow-up assessments were compared

			using the paired Student's *t* test. A p <0.05 was considered statistically significant.
RESULTS Participant flow	13	Flow of participants through each stage (a diagram is strongly recommended). Specifically, for each group report the numbers of participants randomly assigned, receiving intended treatment, completing the study protocol, and analyzed for the primary outcome. Describe protocol deviations from study as planned, together with reasons.	A flow chart was not available
Recruitment	14	Dates defining the periods of recruitment and follow-up.	This article does not show the enrolment periods but does indicate that this study was performed between August 2004 and December 2005.
Baseline data	15	Baseline demographic and clinical characteristics of each group.	All demographic data and baseline characteristics for the 39 post myocardial patients were reported in table 1.
Numbers analyzed	16	Number of participants (denominator) in each group included in each analysis and whether the analysis was by "intention-to-treat". State the results in absolute numbers when feasible (*e.g.*, 10/20, not 50%).	Of 91 patients who were screened for possible enrolment, 37 refused to participate and 15 did not meet the inclusion criteria because of exertional angina (n=3), sustained ventricular arrhythmias (n=3) or exercise-limiting diseases (n=9). The remaining 39 patients were enrolled and were randomly assigned to the 3-month training program (n=20) or to the nontraining group (n=19).
Outcomes and estimation	17	For each primary and secondary outcome, a summary of results for each group, and the estimated effect size and its precision (*e.g.*, 95% confidence interval).	In the training group, exercise capacity increased by 15% (p<0.01), to the same level as in healthy controls. The post-training myocardial perfusion reserve increased in both remote (30%, p<0.01)

			and infarcted myocardium (25%, $p<0.05$) and reached the same level as in healthy controls. The change in exercise capacity correlated with the change in myocardial perfusion reserve in the remote myocardium ($r=0.55$, $p<0.001$ for peak VO_2). In the nontraining group, exercise capacity and myocardial perfusion reserve were unchanged.
Ancillary analyses	18	Address multiplicity by reporting any other analyses performed, including subgroup analyses and adjusted analyses, indicating those pre-specified and those exploratory.	---
Adverse events	19	All important adverse events or side effects in each intervention group.	No patient died, was hospitalized for coronary intervention or had worsening symptoms during the 3-month study period.
DISCUSSION Interpretation	20	Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision and the dangers associated with multiplicity of analyses and outcomes.	Cardiac rehabilitation improves perfusion reserve in both infarcted and remote myocardium, with a parallel increase in exercise capacity.
Generalizability	21	Generalizability (external validity) of the trial findings.	In routine clinical practice, cardiac rehabilitation will begin as soon as possible after a cardiac event. However, studying patients soon after acute myocardial infarction is complicated and given this study purpose and design only patients with stable myocardial infarction were chosen. Moreover, only men were enrolled so further studies should be performed on women. Last but not least, patients were

			treated for 3 months only and the long-term effects of cardiac rehabilitation on these parameters remain unknown.
Overall evidence	22	General interpretation of the results in the context of current evidence.	Three months of cardiac rehabilitation at a moderate intensity resulted in an improvement in exercise capacity to the same level as in healthy controls and rehabilitation also increased myocardial perfusion reserve in both the remote and infarcted myocardium to the same level as in healthy subjects. The change in exercise capacity correlated positively with that the myocardial perfusion reserve in the remote myocardium and left ventricular dimension, function, wall stress or infarct size did not change during the study period.

The Jadad 5-point scale was utilized as an initial screening tool minimizing the likelihood of publication selection bias (Jadad *et al.*, 1996). Articles that were accepted into the analysis of this systematic review achieved a minimum of three out of five in the Jadad scale. Afterwards, the 22-question CONSORT checklist was employed to analyse multiple elements of individual studies that achieved a score of three or more using the Jadad scale. The Jadad scale is appropriate but evaluates three general areas of an investigation while the CONSORT appraises multiple factors which may indirectly affect the results of an investigation.

3.4. Data collection

Data collection included all the possible methods used to identify published and unpublished data to be included in the review, to determine eligibility of the data for inclusion or exclusion and if necessary, to extract data for analysis. The search provided references to books, electronic books, papers and abstracts that were used to obtain articles from the University of Chester library or via interlibrary loans. This material also contained further references to additional literature. In addition, a manual search by examining reference lists from original research papers and review articles was also conducted.

3.5. Statistical analysis

No statistical analysis was performed on the data obtained form the investigation involved in the systematic review. If considered necessary, data was allocated into

tables and graphs to illustrate key points and changes from baseline to follow-up and was portrayed in mean ± standard deviation (± SD) with a 2-tailed statistical significance at a p=0.05 level.

4. Results

4.1. Results of the literature search

The search strategy resulted in 2974 potentially relevant articles. The first selection, which was based only on title, resulted in including 1325 papers. After the identification of duplicate publications and reviewing of the titles and abstracts, 415 papers were identified for possible inclusion and reviewed in full text.

Studies were included if

- the main intervention was aerobic exercise training or an exercise-based cardiovascular rehabilitation programme
- included patients with myocardial infarction or coronary heart disease or coronary artery disease and
- the training program lasted at least two weeks or more.

Moreover, studies were excluded for a variety of reasons, such as inappropriate patient groups, non randomised design, inappropriate intervention(s) and preliminary results available only in an abstract form. The full text evaluation resulted in 18 publications which all met the selection criteria and contained evidence on the key question in patients with myocardial infarction or coronary heart disease or coronary artery disease. Reference tracking yielded two new papers and resulted in inclusion of these additional studies following the same procedures as above. Thus, a total of 20 studies were included in this review, which provided information on a total of 2572

patients with myocardial infarction, coronary artery disease and coronary bypass grafting patients (figure 2).

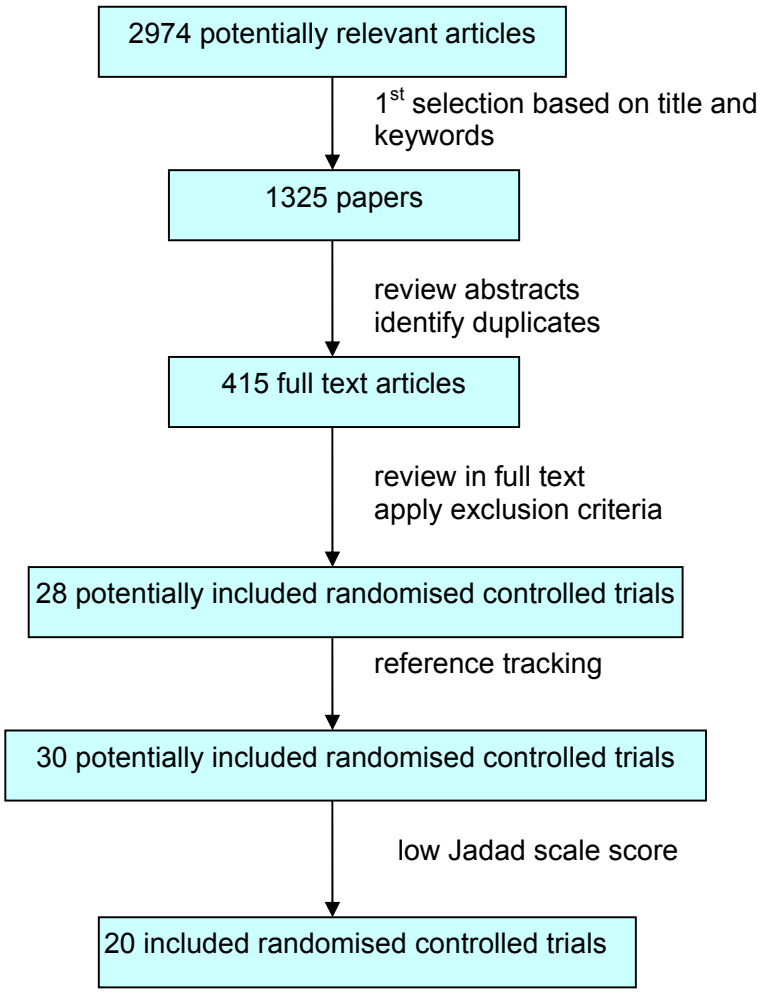

Figure 2. Results of the literature search

4.2. General characteristics

The publication year of the included papers ranged from 1990 up to 2008, with almost half of them published between 2000 and 2008. All the included studies were written in English language. The purpose of 17 studies was the assessment of the effects of aerobic exercise training with different intensities in patients with myocardial infarction and three studies were dealing with patients who had coronary artery disease or coronary heart disease. One study assessed post myocardial infarction patients with signs of moderate depression or anxiety while one trial was a multiple one and assessed both myocardial infarction patients along with individuals who were treated with coronary artery bypass graft surgery.

4.3. Population characteristics

The majority of the studies were carried out with populations from Europe (14 studies out of 20) and from Asia (four trials) and only few from the United States of America (two trials). Sample sizes ranged between 17 and 382 participants, although about half of the studies had a sample size equal or above 150 participants. All of the studies examined adult samples and almost half of them sampled individuals with an age between 60 and 70 years old. Five studies examined subjects aged between 55 and 60 years old while two had a sample above 70 years old. Only five studies comprised of only male population while the authors of three studies have not identified whether the subjects are males or

females. The rest of the studies (14 studies out of 22) have a population of both male and female individuals.

In general, the 2572 subjects were randomised either to a structured program of aerobic exercise training group (n=1270) or to a comparison or control group (n=1133). Approximately, 169 patients were engaged in counselling or some form of community care without any exercise component. Among the 2572 individuals, only 5% were females (n=148) while 55% were males (n=1435). The rest individuals (40% or n=989) were of unrecorded sex.

Table 2.Basic characteristics of the included reviews

Authors (date)	Subjects (sex, age, groups)	Intervention studied	Training protocol (type of exercise)	Duration and frequency of program, duration of session	Intensity	Effects
Amundsen et al.(2008)	17 AMI patients (14♂, 3♀) 2 groups (high=8, 6♂,2♀, moderate=9, 8♂,1♀)	Aerobic treadmill exercise training with different intensities (ie. high or moderate)	Uphill treadmill walking	10 weeks High intensity: 5 min. warm-up, 4x4 min. intervals separated by 3min. pauses, 5 min. cool down Moderate intensity: 41 min.	High inten:50-60% of $\dot{V}O_2$peak, 80-90% of $\dot{V}O2_{PEAK}$ pauses @ 50-60% of $\dot{V}O_2$peak Mod.inten:50-60% of $\dot{V}O_2$peak	↑ $\dot{V}O_2$peak, early diastolic myocardial relaxation rate, peak early diastolic strain rate in the high-intensity group ↔rest HR, peak HR for both groups ↑peak early diastolic mitral flow velocity for both groups
Bethell & Mullee (1990)	200 ♂ AMI patients, 2 groups (treat=99, control=101)	Exercise training only	Circuit training @8 stages: bicycling, stepping, overhead pull, squat lift, trunk curls, quadriceps, bench press, sitting leg press	3 months 3 times/week 20 to 30 min.	70% to 85% of predicted HRmax	↔ frequency in HRresting, blood cholesterol, triglycerides ↑predicted $\dot{V}O_2$max, energy level in treat. group ↓DP in peak exercise in treat. group
Carlsson (1998)	382 patients,s1: n=177,121 AMI (in=61,con=60) 56 CABG (in=27, co=29) s2:n=205,142 AMI(in=75, c=67),63 CABG (in=31, c.=32)	Exercise training or usual follow-up	Regular exercise program of easy training (before randomiz.) Continuous physical exercise program (after randomiz.)	30 min. (before randomization) 2-3months 2-3 times/week 60 min. (after randomization)	Not mentioned	↑ work capacity except AMI control ↓total cholesterol, LDL, BMI for the AMI intervention group ↓total cholesterol, LDL for the CABG intervention group

Table 2.Continued

Authors (date)	Subjects (sex, age, groups)	Intervention studied	Training protocol (type of exercise)	Duration and frequency of program, duration of session	Intensity	Effects
Dugmore et al. (1999)	124 AMI patients (122♂, 2♀) groups (rehab=62, control=62) Good prog.group =36 p. Poor prognosis group=26 patients	Exercise only	Aerobic training and local muscular endurance training	12 months 3 times/week	50 to 65% of $\dot{V}O_2$peak (poor prognosis group) 65 to 80% of $\dot{V}O_2$peak (good prognosis group)	↑RPP, $\dot{V}O_2$peak, exercise time, cardiorespiratory fitness in treatment group
Eto et al. (2004)	36 AMI patients (35♂, 1♀) 2 groups (training=18, control=18)	Exercise only	Supervised bicycle exercise	2 weeks 2 times/day 30 min	constant workload at the anaerobic threshold level[1]	↑workload, $\dot{V}O_2$peak, $\dot{V}O_2$ @anaerobic threshold, cardiac index @ peak exercise,$PETCO_2$
Gunning et al. (2002)	25 AMI patients(23 ♂, 2♀) 2 groups (training=15, control=10)	Exercise only	Supervised aerobic exercise programme by ergometer or circuit routine	6 weeks 2 times/week 40 min	60% to 80% of age predicted HRmax	↑myocardial perfusion characteristics
Hambrecht et al. (2000)	19 ♂ CAD patients, 2 groups (rehabilitation=10, control=9)	Exercise only	Bicycle ergometer	4 weeks 6 times/day 20 min	80% of HRmax[2]	↑in coronary blood-flow velocity in rehab group ↑ flow-dependent dilatation

[1] as determined by the exercise testing
[2] as reached during peak oxygen uptake in the initial exercise test

Table 2.Continued

Authors (date)	Subjects (sex, age, groups)	Intervention studied	Training protocol (type of exercise)	Duration and frequency of program, duration of session	Intensity	Effects
Izawa et al. (2006)	24 AMI patients, 2 groups (training=12, control=12)	Unsupervised exercise training maintenance after CR	Low intensity muscle strength training(4 sets of 5 rep./session) and walking	6 months 2 times/week 60 min	Perceived exertion rating of 11 to 13 on the 6 to 20 Borg scale	Exercise capacity and increase in muscle strength were maintained
Lee et al. (2008)	39 AMI patients 2 groups (interv=20, control =19)	Exercise only	Aerobic exercise	3 months 3 times/week 30 min.	55% to 70% of the $\dot{V}O_2$peak [3] and a perceived exertion rating of 12 to 13 on the Borg scale	↑ $\dot{V}O_2$max, maximal workload, MPR in the remote+infarcted myocardium,hyperemic perfusion index in the intervention group, ↓rest RPP, perfusion index at rest in the intervention group ↔ exercise capacity, rest HR, rest SBP, rest RPP, peak HR, peak SBP, peak RPP, MPR, perfusion indices in the control group ↔LV mass, volume, end-diastolic volume/mass ration, end-systolic wall stress, cardiac index, infarct size in both groups

[3] as measured in the initial exercise test

Table 2.Continued

Authors (date)	Subjects (sex, age, groups)	Intervention studied	Training protocol (type of exercise)	Duration and frequency of program, duration of session	Intensity	Effects
Leizorovicz et al. (1991)	182 ♂ AMI patients, 3 groups (rehab=60, community care=61, control=61)	Rehabilitation program, counselling programme without exercise training or usual care program	Exercise test on a cyclo-ergometer	6 weeks 3 times/week 25 min.	80% of the HRmax[4]	↑exercise tolerance in rehab group ↑return to work ↓smokers in rehab group ↔ deaths in rehab group
Marchionni et al. (2003)	270 MI patients (183♂, 87♀) 3 groups (hospital-cr=90, home-cr=90, control=90)	Hospital-based CR, home-based CR or no CR	Endurance training and stretching and flexibility exercises	2 months 3 times/week endurance and 2 times/week stretching 35 min.	70-80% of HR[5]	↑total work capacity in the hosp-cr group and home-cr group ↑ total work capacity in middle-aged men and old patients
Maroto Montero et al. (2005)	180 ♂ low-risk AMI patients , 2 groups (cr program=90, control=90)	Physical training, psychological program (group therapy), education program (risk factors modification), return to work counselling	Physiotherapy and aerobic training on mats or an exercise bicycle	3 months 3 times/week 60 min	75% of the maximum achieved HR (first 6 weeks) 85% of the maximum target HR (last 6 weeks)	↓ CV mortality, complications (esp.revascularization, unstable angina, heart failure) modification of lifestyle behaviours better fulfilment of therapeutic guidelines

[4] as evaluated by the baseline test
[5] attained during baseline symptom-limited exercise test

Table 2.Continued

Authors (date)	Subjects (sex, age, groups)	Intervention studied	Training protocol (type of exercise)	Duration and frequency of program, duration of session	Intensity	Effects
Oldridge et al. (1990)	201♂ low risk with AMI and moderate depression or anxiety, 2 groups (treat=99, control=102)	Exercise training and behavioural counselling	Aerobic exercise	8 weeks 2 times/week 50 min.	65% of the HRmax[6]	↑exercise tolerance ↓state of anxiety or depression
Ornish et al. (1990)	41 CAD patients (36 ♂, 5♀), 2 groups (intervention=22, 21♂, 1♀, control=19, 5♂,4 ♀)	Experimental group (low-fat vegetarian diet, stopping smoking, stress management training and moderate exercise	Exercise	12 months minimum of 3h/week 30 min/session within target HR	50% to 80% of HR[7] or 50% to 80% of their age-adjusted HRmax[8]	↑ frequency, duration, severity of angina in the control group ↓total cholesterol, LDL, frequency, duration, severity of angina in the intervention group improvement in the severely stenosed lesions
Speecchia et al. (1996)	256 AMI patients, 2 groups (inter=125, control=131)	Exercise only	Bicycle ergometer and callisthenics	4 weeks 5 times/week 30 min.	Graded according to 75% of maximal work capacity[9]	Trained patients with EF <41% had better outcomes than untrained

[6] as achieved during the exercise test
[7] at which 1mm ST segment depression occurred during baseline treadmill test
[8] based on level of conditioning
[9] reached in previous exercise test

Table 2.Continued

Authors (date)	Subjects (sex, age, groups)	Intervention studied	Training protocol (type of exercise)	Duration and frequency of program, duration of session	Intensity	Effects
Stähle et al. (1999)	101 patients (81♂,20♀) 2 groups (training=50, 41♂, 9♀, AMI=29, Angina=21, control=51,40♂, 11♀ AMI=31, Angina=20)	Outpatient aerobic group-training programme	Aerobic exercise engaging large muscle groups	3 weeks 3 times/week 50min	exercise inten.of ≥50% based on the relation between HRmax and $\dot{V}O_2$max for 40 min, ≥80% of the estimated $\dot{V}O_2$max during 3 periods of 3-4 min	↑exercise capacity, maximal exercise capacity for the training group ↓RPE score @30%, @ 60% of maximal exercise capacity, @ maximum identical workload for the training group
Taylor (1997)	54 MI patients (47♂,7♀), 3 groups (exercise+education= 18,14♂,4♀, education only=18,16♂,2♀, control=18,17♂,1♀)	Aerobic exercise training program+ weekly discussion/information session, discussion and information only group, control group	Individually prescribed aerobic training program	6 weeks 3 times/week 30 min.	HR equivalent to 40-50% of measured $\dot{V}O_2$max[10]	↓anxiety, depression for all groups ↑ walking activity, return to function, rehab. status for the exer.group
Tsoukas, Andonakoudis & Christakos (1995)	100 AMI patients (91♂, 9♀), 2 groups (intervention=60,56♂, 4♀, control=40,35♂,5♀)	Ergometric bicycle	Modest bicycle exercise training with increasing intensity	3 months 4 times/week 5 periods of 5 min. with 2-min. intervals	Every 4 sessions 10% gradual increase	↓SBP, HR, DP in treat.group [11], ↑ exercise time, exercise tolerance in

[10] determined from treadmill exercise tolerance test

[11] as measured at the 3rd and 5th minute of the submaximal treadmill stress test according to Bruce protocol

						treat.group

Table 2.Continued

Authors (date)	Subjects (sex, age, groups)	Intervention studied	Training protocol (type of exercise)	Duration and frequency of program, duration of session	Intensity	Effects
Vona et al. (2004)	52 AMI patients (40♂, 12♀)2 groups (treatment=28, 21♂,7♀, control=24, 19♂, 5♀)	Exercise only	Moderate aerobic training	3 months 3 times/week 60 min	75% of peak exercise HR[12]	↑HDL, function capacity, METs in the treatment group ↔ HDL, function capacity, METs in control group
Yu et al. (2004)	269 patients (AMI=193, PCI=76) 2 groups (cardiac rehabilitation program=181, AMI=129, PCI=52, control=88, AMI=64, PCI=24)	Outpatient exercise and education program (in 3 phases)	Aerobic cardiovascular training (stretching, treadmill, ergometry, rowing, stepping, dumbbell or weight training)	8 weeks 2 times/week 120 min	65% to 85% of age-adjusted HRreserve[13]	↓progression of resting DF in the CR group ↑LV diastolic indices, exercise capacity in the CR group

AMI=acute myocardial infarction, BMI=body mass index, CABG=coronary artery bypass graft, CAD=coronary artery disease, CR=cardiac rehabilitation, CV=cardiovascular, DF= diastolic function, EF=ejection fraction, HDL=high density lipoprotein, HR=heart rate, LDL=low density lipoprotein, LV=left ventricular, METs=metabolic equivalents, MPR=myocardial perfusion reserve, PCI=percutaneous coronary intervention, $PETCO_2$=pressure of end-tidal CO_2 RPE=rating of perceived exertion, RPP or DP=rate-pressure product or double product, SBP=systolic blood pressure, $\dot{V}O_2max$=maximum oxygen consumption, $\dot{V}O_2peak$ =peak oxygen consumption

[12] as measured in the second electrocardiographic stress testing
[13] based on the American College of Sports Medicine (ACSM) guidelines for exercise testing and prescription

4.4. Exercise-based rehabilitation program results

Exercise aerobic training is relatively safe for the vast majority of appropriately assessed cardiovascular patients (American College of Sports Medicine [ACSM], 2006). An exercise prescription is the process for systematically recommending to a patient an individualized aerobic exercise programme to help promote optimal physiological and health benefits from the training (Leon, 2000). The essential components of a systematic and individualized exercise prescription include the appropriate mode or modes, intensity, duration, frequency and progression of physical activity (ACSM, 2006, Froelicher & Myers, 2006). These five components apply when developing exercise prescriptions for people of all ages and fitness levels, regardless of the individual's health status (ACSM, 2006).

However, the exercise prescription should be developed with careful consideration of the individual's health status (including medications), risk factor profile, behavioural characteristics and personal goals and last but not least his or her exercise preferences (ACSM, 2006). An exercise stress test is a useful tool in order to determine functional capacity (ACSM, 2006) and all coronary artery disease patients should undergo a symptom-limited exercise stress test before referral to an exercise-based cardiovascular rehabilitation programme (Thompson, 2005). This is in order to establish a baseline, to determine maximal heart rate (HRmax) and to exclude important ischaemia, symptoms or arrhythmias that would alter the therapeutic approach (Thompson, 2005). Therefore, this testing should be performed with

patients on their usual medications (for example beta-blockers) to match the conditions likely to be encountered during the exercise sessions (Thompson, 2005).

For aerobic training, the magnitude of the stress is quantified by the intensity, measured as the percent maximum oxygen consumption (% of $\dot{V}O_2$max) or by percent of maximal heart rate (% of HRmax), the duration of the training session measured by time (minutes) and the frequency measured as training sessions per week (Thompson, 2005). Many of these methods are found in nationally and internationally recognised guidelines, including:

- the Scottish Intercollegiate Guidelines Network (SIGN, 2002)
- the British Association for Cardiac Rehabilitation (BACR, 2003)
- the American Association for Cardiovascular and Pulmonary Rehabilitation (AACVPR, 2004)
- the American College of Sports Medicine (ACSM, 2006) (Buckley, 2006).

Consequently, and with very few exceptions, most exercise training studies in cardiovascular patients have patients exercise at least three times per week for at least 20 minutes at heart rates corresponding between 60% and 85% of maximum heart rate although even lower intensities may produce a training response (Shepard & Balady, 1999, Froelicher & Myers, 2006). In general, the mode of exercise must involve movement of large muscle groups such as is required for example by bicycling, walking, running, skating, cross-country skiing, swimming and the like (Froelicher & Myers, 2006).

Intensity

Much of the art of exercise prescription involves individualising the exercise intensity (Froelicher & Myers, 2006). Exercise intensity is felt to be the most important of the four main components of the principle of training (McArdle, Katch & Katch, 2006). Intensity and duration of exercise determine the total caloric expenditure during a training session and are inversely related (ACSM, 2006). For example, improvements in health related benefits may be achieved by a low intensity, longer duration regimen whereas improvements in cardiorespiratory fitness ($\dot{V}O_2max$) are associated with a higher intensity, shorter duration program (Barnard *et al.*, 1973 as cited by ACSM, 2006). The prescribed exercise intensity for each cardiac patient should be above a minimal level required to induce a "training effect", yet below the metabolic load that could evoke abnormal clinical signs or symptoms, such as onset of angina pectoris, ventricular arrhythmias, plateau or decrease in systolic blood pressure, significant electrocardiographic disturbances like ischemic ST segment depression and others (Franklin, Gordon & Timmis, 1992, ACSM, 2006).

Setting the safe upper limit for exercise intensity should be a foremost consideration, regardless of the methods employed and should be established in order to prevent the signs and symptoms mentioned above (ACSM, 2006). Typically, exercise intensity is expressed as a percentage of the maximal capacity in absolute terms (i.e. workload or watts) or relative to the maximal heart rate (HRmax), maximum oxygen uptake ($\dot{V}O_2max$) or rating of perceived exertion on the 6 to 20 Borg scale (RPE) (Froelicher & Myers 2006). The capacity of the body to deliver and utilize

oxygen is expressed as the maximal oxygen uptake ($\dot{V}O_2max$) and is defined as the product of maximal cardiac output ($\dot{Q}max$) and maximal arteriovenous oxygen difference [$(a-\bar{v})O_2$ diff max] (Froelicher & Myers, 2006).

Because heart rate and oxygen consumption are linearly related during dynamic exercise involving large muscle groups, a pre-determined training or target heart rate (THR) has become widely used as an index of exercise intensity in a variety of clinical populations, including cardiac patients (Wilmore, 1976 as cited by ACSM, 2006). The heart rate reserve method appears to closely approximate the same percentage of the oxygen uptake reserve (% of $\dot{V}O_2$reserve) in cardiovascular patients (Brawner, Keteyian & Ehrman, 2002, Franklin & Swain, 2003) and the minimal effective intensity for improving cardiorespiratory fitness approximates 45% of the minimum oxygen uptake reserve ($\dot{V}O_2$reserve) (Swain & Franklin, 2002). However, the intensity should ideally be related to the individual's previously determined peak oxygen consumption because the proportion of peak oxygen consumption represented by a particular bout of exercise dictates the level of the metabolic and physiological responses that will be elicited (British Association for Cardiac Rehabilitation [BACR], 2003).

In general, exercise during conditioning sessions, should be within the range of 40% to 85% of functional capacity (ACSM, 2006) and typically, cardiac patients beginning an exercise programme will need to start at 40% to 60% of $\dot{V}O_2$peak (BACR, 2003). The intensity should be at least 50% of an individual's maximal oxygen uptake ($\dot{V}O_2max$) (typically ranging from 60% to 80%) and the percentage of $\dot{V}O_2max$

required can be approximated by heart rate or by level of perceived exertion on the 6 to 20 Borg scale (Froelicher & Myers, 2006). Training benefits have been demonstrated to occur when using exercise intensities ranging from 40% to 85% of $\dot{V}O_2$max, which usually are equivalent to 50% to 90% of maximal heart rate (Froelicher & Myers, 2006). Ordinarily, the most appropriate intensity for most patients in exercise-based cardiovascular rehabilitation programmes is 60% to 70% of maximal capacity (Froelicher & Myers, 2006). Gains in aerobic fitness are modest until the intensity approximates 50% to 60% of $\dot{V}O_2$max, at which time improvement is rapid (Franklin & Fardy, 1998). To achieve improvement in cardiorespiratory endurance, the intensity of aerobic exercise should be maintained between 40% and 85% of $\dot{V}O_2$max or functional capacity (generally corresponding to about 50% and 90% of maximal heart rate, respectively) (Leon, 2000)(table 3).

Table 3. Recommended aerobic exercise intensities relative to the percentage of maximal oxygen uptake (% $\dot{V}O_2$max), maximal heart rate reserve (% HRRmax) and maximal heart rate (%HRmax) (adapted from Buckley, 2006).

Guidelines	ACSM (1994,2000,2006)	BACR (1995,2003), SIGN (2002)
% $\dot{V}O_2$max*	40%-85%	40%-60%†
% HRRmax	40%-85%	40%-60%†
% HRmax	55%-90%	60%-75%†

* The term $\dot{V}O_2$max is used in this case for reasons of simplicity but it must be noted that guidelines vary in the use of $\dot{V}O_2$peak or maximal $\dot{V}O_2$reserve.

† In Britain the upper intensity limit is lower than for the USA because British programmes do not typically use sophisticated ECG heart rate monitoring during the actual exercise sessions, except in cases of higher risk patients.

Most studies presented here use heart rate as a means of controlling intensity but this requires the availability of a well organised facility to establish the relationship between heart rate and oxygen uptake (up to $\dot{V}O_2$peak) for the participants. Since heart rate generally correlates well with oxygen uptake and coronary blood flow, it is commonly used in exercise prescription as an indicator of exercise intensity (Leon, 2000). Therefore, the threshold intensity for initial improvement in aerobic capacity lies between 40% and 60% of $\dot{V}O_2$max (Leon, 2000). However, it is generally not necessary to engage in vigorous activity in order to derive many of exercise's benefits. Nevertheless, this way, i.e. using heart rate as a control mean for intensity, is convenient in that equivalent percentages of maximal heart rate and $\dot{V}O_2$peak are numerically equal, for example 70% to 85% of the maximal heart rate is known to be equivalent to about 60% to 80% of $\dot{V}O_2$peak (BACR, 2003). The numerical difference is attributable to the fact that as maximal effort is approached, oxygen uptake increases relatively less than heart rate (BACR, 2003).

However, what should be noted is the fact that the intensities used in all the different regimes reviewed are just above the maximal percentage of $\dot{V}O_2$peak or maximum heart rate. In the studies reviewed all of the intensities were determined by an exercise stress testing conducted at baseline before or after randomization, except in a study by Carlsson (1998) where the intensity of the exercise rehabilitation program was not mentioned even though all patients underwent an exercise stress test on an electronically controlled resistance bicycle ergometer. Eto and colleagues (2004) assessed 36 patients after an acute myocardial infarction through a supervised bicycle exercise program where the intensity was determined by the

anaerobic threshold level. The anaerobic threshold has been classically defined as the exercise intensity at which energy production shifts from primarily aerobic to anaerobic (non-oxidative) metabolism (Cerny & Burton, 2001). Healthy sedentary individuals reach this point at about 70% of the $\dot{V}O_2$max (Cerny & Burton, 2001) while for coronary heart disease patients anaerobic threshold commonly occurs at about 60% of $\dot{V}O_2$max or about 70% of the peak heart rate (Leon,2000).

A few researchers used alone, or in combination the perceived exertion rating on the 6 to 20 Borg scale. Cardiorespiratory and metabolic variables are strongly related to the rating of perceived exertion such that the ratings are a reproducible and valid indicator of intensity of steady state exercise (BACR, 2003). On the 6 to 20 Borg scale, a rating of 11 or 12 to 13 (interpreted as "fairly light" to "somewhat hard") corresponds to approximately 60% of the heart rate range or $\dot{V}O_2$peak (BACR, 2003). Generally, aerobic exercise rated as 11 to 13 (on the 6 to 20 Borg scale), between "fairly light" and "somewhat hard", corresponds to the upper limit of prescribed training heart rates during the early stages of outpatient exercise-based cardiac rehabilitation programs (ACSM, 2006). For higher intensity levels of aerobic exercise training, rating of perceived exertion of 14 to 16 may be appropriate provided there are no signs or symptoms of ischemia or serious arrhythmias (ACSM, 2006) (table 4).

Table 4.Rating of perceived exertion (RPE): 15-point category scale (adapted from Borg, 1973).

6	
7	Very, very light
8	
9	Very light
10	
11	Fairly light
12	
13	Somewhat hard
14	
15	Hard
16	
17	Very hard
18	
19	Very, very hard
20	

A reduced heart rate and blood pressure for a given work intensity in myocardial infarction patients have been demonstrated (Bethell & Mullee, 1990). Studies by Leizorovicz et al. (1991) and Tsoukas, Andonakoudis & Christakos (1995) also reported reductions in exercise heart rate and systolic blood pressure for a given workload following six weeks and three months of regular exercise training, respectively. The rate pressure product, which is an indication of myocardial oxygen consumption, fell in a group of 99 myocardial infarction patients following a three month controlled exercise programme (Bethell & Mullee, 1990). The control group of the same study showed no change in rate pressure product (Bethell & Mullee, 1990).

Moreover, after 12 months of training, 62 acute myocardial infarction patients showed an increase in rate-pressure product and oxygen uptake at peak exertion

(Dugmore *et al.*, 1999). This might have been partly to a direct improvement in cardiorespiratory fitness (Dugmore *et al.*, 1999). The improvement in cardiorespiratory fitness in the poor prognosis patients with regular exercise training was particularly encouraging, illustrating the effectiveness of low and moderate intensity aerobic training in higher risk groups such as the one group that participated in the study (Dugmore *et al.*, 1999).

Conversely, a trial by Leizorovicz et al. (1991) found no significant fall in double product with exercise. They suggested this might show a habituation effect of exercise rather than an aerobic training effect (Leizorovicz *et al.*, 1991). However, their exercise programme lasted only six weeks, which might have been too short in order to allow a training effect to develop. Thus, the increased workload in the rehabilitation program group apparently indicated better effectiveness after rehabilitation: similar level of “cardiac work” for a higher peripheral muscular work (Leizorovicz *et al.*, 1991). Aerobic exercise training allowed a higher workload without excessively increasing the heart rate and heart rate x systolic blood pressure product, i.e. the oxygen consumption (Leizorovicz *et al.*, 1991). The mechanisms of this improvement have been attributed to a better peripheral tissular oxygen extraction (Leizorovicz *et al.*, 1991).

The index of relative cardiac work, called the double product or rate-pressure product closely reflects directly measured myocardial oxygen uptake and coronary blood flow over a range of exercise intensities (McArdle, Katch & Katch, 2006).The reduction of exercise induced heart rate and systolic blood pressure (measured at the brachial artery) produced by exercise training of cardiac patients is a very

important effect (Bethell & Mullee, 1990) because the heart rate x systolic blood pressure product (the double product or rate pressure product) is a direct reflection of myocardial workload and oxygen demand and provides a convenient estimate of myocardial workload (oxygen uptake) (McArdle, Katch & Katch, 2006). Aerobic exercise training consistently results in a reduction during submaximal physical exertion in heart rate, systolic blood pressure and the heart rate x systolic blood pressure product (Leon, 2000). Since rate pressure product is a major determinant of myocardial oxygen requirements and coronary blood flow, this adaptation allows a higher intensity of physical exertion to be performed prior to reaching the threshold for myocardial ischaemia and associated angina pectoris (Leon, 2000).

Amundsen and colleagues (2008) studied the effects of moderate intensity exercise (50% to 60% of $\dot{V}O_2$peak) versus high intensity exercise (80% to 90% of $\dot{V}O_2$peak with pauses at 50% to 60% of $\dot{V}O_2$peak) in a total of 17 myocardial infarction patients. After ten weeks, both groups showed an increase in peak early diastolic mitral flow velocity (Amundsen *et al.*, 2008). However, the increase in $\dot{V}O_2$peak was significantly higher in the high intensity group (Amundsen *et al.*, 2008). The authors concluded that aerobic treadmill exercise training with high, but not moderate, intensity is superior for improving $\dot{V}O_2$peak (Amundsen *et al.*, 2008).

All the researchers used the intensity percentage range suggested by the American College of Sports Medicine (2006) or the British Association for Cardiac Rehabilitation (2003). But how hard must someone push himself or herself in order to gain benefits is not clearly defined. Evidence nowadays suggests that in most

studies reporting health-related benefits from regular physical activity were involved in relatively low-intensity exercise (Franklin & Fardy, 1998). Vigorous physical training by increasing myocardial oxygen consumption and simultaneously shortening diastole and coronary perfusion time may evoke a transient oxygen deficiency (Franklin & Fardy, 1998).

Duration

The duration of an exercise session interacts with the intensity to result in the expenditure of a sufficient number of calories in order to achieve health and fitness goals, such as an improved body composition (ACSM, 2006). Exercise duration cannot be discussed appropriately without also discussing exercise intensity (Wilmore & Costill, 2004). Therefore, it should be noted that there is an inverse relationship between the duration and the intensity of aerobic exercise required to improve an individual's cardiorespiratory fitness (Leon, 2000).

The higher the intensity of exercise, the shorter the duration required for a training effect and, conversely, low intensity exercise may be compensated for by a longer duration of exercise sessions (Leon, 2000). Lower intensity activity should be therefore, done for a longer period of time (30 minutes or even more) (ACSM, 2006). Exercise training for five to ten minutes could improve aerobic capacity whereas a 30-minute session is even more effective (Franklin & Fardy, 1998). People training at a low intensity should conduct the exercise sessions over a longer period of time (30 minutes or more as mentioned previously) and, conversely, individuals training at higher levels of intensity may train for 20 minutes or less (ACSM, 2006). This

difference was highlighted in a study by Amundsen and colleagues (2008) where the high intensity group trained for approximately 25 minutes while the moderate intensity group walked for 41 minutes, which equated the total oxygen uptake per session in the two groups.

The duration of the cardiac rehabilitation conditioning period (exclusive of warm-up and cool-down) needs to be short initially but increases progressively to, typically, 20 to 60 minutes of continuous or intermittent activity (e.g. ten minutes of bouts accumulated throughout the day) (BARC, 2003, ACSM, 2006).The ACSM position stand recommends a minimum of 20 minutes of cardiovascular exercise for improvement in aerobic capacity (Pollock, Gaesser & Butcher, 1998). So, an optimal duration of an exercise session is considered to be in the range of 30 to 60 minutes (Froelicher & Myers, 2006). A minimum of 20 minutes per session at an exercise intensity of 50% to 85% of $\dot{V}O_2$max appears necessary to improve $\dot{V}O_2$max (Leon, 2000). Only one study, which was conducted by Hambrecht et al. (2000), prescribed exercise training for 20 minutes, while the majority of the authors prescribed exercise training from 30 to 60 minutes. None of the studies reviewed here had an exercise time greater than 60 minutes, since an optimal duration of an exercise session for increasing physical fitness is considered to be in the range of 30 to 60 minutes (Froelicher & Myers, 2006). Moreover, in one study by Dugmore and colleagues (1999) the duration of each session was not mentioned.

Shorter sessions are less effective and longer sessions might increase the risk of musculoskeletal injury, cardiovascular incidences and lower compliance (Bethell,

2006). Most exercise-based cardiovascular rehabilitation programmes use a one hour sessions, including five to ten minutes of warm-up and five to ten minutes of cool-down periods (Bethell, 2006). Since the duration of an exercise program is inversely related to the intensity of the activity, lower intensity activity should be done for a longer period of time (30 minutes or more) (ACSM, 2006). Moderate intensity and moderate duration (20 to 30 minutes) exercise is recommended for improving aerobic capacity (i.e. $\dot{V}O_2$max) of most adults (ACSM, 2006). Similar improvements in aerobic capacity are gained with either a short duration of high intensity program or a long duration of low intensity program (Wilmore & Costill, 2004).

This is well manifested among the studies. Researchers that prescribed aerobic training in low intensities had exercise sessions lasting 30 minutes or more, such as Izawa et al. (2006) who prescribed exercise intensities of a perceived exertion rating of 11 to 13 ("fairly light" to "somewhat hard") on the 6 to 20 Borg scale (which corresponds to approximately 60% of the heart rate range or $\dot{V}O_2$peak) and each exercise session lasted 60 minutes, while researchers who prescribed higher exercise intensities had sessions lasting less that 30 minutes, such as the study by Leizorovicz et al. (1991) who prescribed exercise intensities at 80% of maximal heart rate and each session lasted 25 minutes.

Type (mode)

Cardiovascular patients should be encouraged to engage in multiple activities to promote total physical conditioning (i.e. treadmills, cycle ergometer, arm ergometers,

stair climbers and rowing machines) including range-of-motion exercise and resistance training, if medically appropriate (ACSM, 2006). Exercises for the endurance phase employ large muscle groups in activities that are rhythmic or dynamic in nature (ACSM, 2006). Continuous training, as the name implies, involves uninterrupted activity, usually performed at a constant submaximal intensity (BACR, 2003). The greatest improvements in $\dot{V}O_2$max occur when exercise involves the use of large muscle groups over prolonged periods in activities that are rhythmic and aerobic in nature, such as walking, hiking, running, machine-based stair climbing, swimming, elliptical activity, cycling, rowing, combined upper and lower body ergometry, dancing, skating, cross-country skiing, endurance games (ACSM, 2006). The advantage of this is the ease with which intensity may be prescribed and monitored (BACR, 2003).

Endurance (or aerobic) exercise should be the major component of the exercise regimen for coronary heart disease patients (BACR, 2003). Aerobic exercise involves predominantly movement with little strength (e.g. walking, cycling, jogging or swimming) (Bethell, 2006). Myocardial infarction patients undergoing a training protocol of low intensity muscle strength training and walking demonstrated an increase in exercise capacity and in muscle strength at a fixed submaximal work load, suggesting increased mechanical efficiency (Izawa *et al.*, 2006). However, strength-and-endurance exercise involves strength with little movement (e.g. weight lifting) and very intense strength training can raise blood pressure and is not advised for cardiac patients (Bethell, 2006).

Cardiovascular patients benefit from a mixture of aerobic and muscular strength-and-endurance exercise, which are usually alternated on a circuit training program. The advantage of circuit or interval training is that patients get variety in modes of exercise, using cycle and arm ergometers, bench stepping and rowing machines, working on each piece of equipment for a few minutes. A rest period can follow each station if required and this may be particularly important in the early stages of recovery. A further advantage of a circuit is that most large muscle groups of the body can be exercised. Various authors have demonstrated significant improvements in physical work capacity following circuit-interval training, such as Bethell & Mullee (1990), Gunning et al. (2002) and Yu et al. (2004).

Frequency

Favourable training responses have generally been demonstrated when exercise is carried out in the course of at least three to five sessions per week (Froelicher & Myers, 2006). Exercising at least three days a week generally initiates adaptive changes in the aerobic system (McArdle, Katch & Katch, 2006). For those exercising at 60% to 80% of heart rate reserve or 77% to 90% of maximum heart rate, an exercise frequency of three days per week is sufficient to improve or maintain $\dot{V}O_2max$ (ACSM, 2006). For those exercising at the lower end of the intensity continuum, exercising more than three days per week may be needed (ACSM, 2006).

Additional benefits of training six or more days per week appear to be minimal (ACSM, 2006). This does not mean that six or even seven days per week will not give additional benefits but simply for the health related benefits, the optimal gain is achieved with a time investment of three to five days per week. The usual prescribed frequency of exercise sessions for coronary heart disease patients is three to five sessions per week and this is based on the demonstration that increases in $\dot{V}O_2$max with training appear to plateau with three to five days per week of frequency of training (Leon, 2000). Studies that have demonstrated a training effect included aerobic exercise training at least three times per week (Taylor, 1997, Stähle *et al.*, 1999, Vona *et al.*, 2004, Maroto Montero *et al.*, 2005, Lee *et al.*, 2008). An exercise frequency of four to five times or even six times per week may post a challenge for less committed patients or create a conflict with their other interests, if any. In studies with a frequency of sessions more than five times per week the aerobic benefits appeared to be minimal, whereas the incidence of lower extremity injuries might increase abruptly.

The minimum length of a program may be six weeks, but is generally eight weeks and some may last up to 12 weeks (three months) but most of the training effect occurs in the first six to eight weeks. Recent literature has shown that two to three times per week for a minimum of eight weeks (i.e. two months) and ideally a six-month period of supervised exercise is sufficient to achieve physiological benefits and psychological adaptations (SIGN, 2002, American Association of Cardiovascular and Pulmonary Rehabilitation [AACVPR], 2004, Froelicher & Myers, 2006). Only one study reported results after one year (Dugmore *et al.*, 1999) and another one had

follow up data for ten years (Maroto Montero *et al.*, 2005). Therefore, the longer term studies have shown greater improvements in physical fitness from patients but do demand considerable commitment and compliance from cardiovascular patients.

No correlation was found though among session frequency, session duration, exercise intensity, program duration and functional improvement. In the 20 included randomised controlled trials, the frequency of exercise training varied from two up to six sessions per week. The most common frequency was three times a week and the second most common frequency was five times a week. Surprisingly, the improvement in exercise tolerance was not affected by the frequency of training. The intensity of exercise affected the exercise tolerance and some studies demonstrated a greater improvement in exercise from higher exercise intensity. The most common duration of exercise training was eight to twelve weeks and studies with this exercise duration showed significant improvement in exercise tolerance. The duration of each session lasted from 20 minutes up to 60 minutes while the intensity varied from 40% up to 85% of HRmax.

When it comes to the benefits of regular exercise, increased cardiorespiratory fitness is often emphasized more than the potential for improved health and disease prevention (Franklin & Fardy, 1998). Gunning et al. (2002) provided evidence to support the value of aerobic exercise training following myocardial infarction as a means of stimulating improved myocardial perfusion in the infarcted zone. Thus, the benefits of aerobic exercise are not only a consequence of peripheral physiological adaptation, but are a result of direct effects on myocardial perfusion (Gunning *et al.*, 2002). Lee and colleagues (2008) demonstrated that after 3 months of a cardiac

rehabilitation program at a moderate intensity (55% to 70% of $\dot{V}O_2$peak) resulted in an improvement in exercise capacity and the same cardiac rehabilitation program also increased myocardial perfusion reserve in both the remote and infarcted myocardium. Since exercise capacity is known to be an important prognostic factor in patients with cardiovascular diseases, these findings suggest the survival benefit of cardiac rehabilitation as well as the need for exercise-based cardiovascular rehabilitation programs (Lee *et al.*, 2008).

The hemodynamic consequences of an aerobic exercise program include a decrease in resting heart rate, a decrease in the heart rate and systolic blood pressure at any matched submaximal workload, an increase in total work capacity and maximal oxygen uptake and a faster recovery from a bout of exercise (Froelicher & Myers, 2006). But these hemodynamic responses to exercise are greatly affected by the type of exercise being performed, by whether or not disease is present and by the age, gender, and fitness of the individual (Froelicher & Myers, 2006). Compared with no cardiac rehabilitation, post myocardial cardiac rehabilitation programs enhance exercise tolerance in patients of all ages, including those older that 75 years and as old as 86 years, who have been excluded from most previous trials (Marchionni *et al.*, 2003). Total work capacity improved consistently more with treatment in middle-aged men and old patients than in very old patients, and this observation would not have been detected without having enrolled patients older than 75 years (Marchionni *et al.*, 2003). Exercise in the elderly can improve functional capacity in patients more than 65 years of age and the elderly show greater improvement in functional capacity than younger patients

enrolled in similar programmes of exercise (Ades *et al.*, 1990). Study findings from a non randomised comparative study that was conducted in a sample of 283 patients showed that older coronary patients respond to aerobic conditioning with remarkable improvements in submaximal endurance capacity (Ades *et al.*, 1993). As one can understand, older patients are in greater need of these programmes because they become deconditioned more easily as a result of a cardiovascular disease (Ades *et al*., 1993).

Most of the biological changes from aerobic physical training either decrease the oxygen demand or increase the supply of myocardial oxygen (Carlsson, 1998). Physiological training may promote prevention of coronary artery disease by the following biological mechanisms:

- increase myocardial supply
- increase myocardial function
- increase electrical stability of myocardium and
- decrease myocardial work and oxygen demand (Carlsson, 1998).

The appreciable fall by 14% in the submaximal double product demonstrated among the patients of the treatment group in the study by Bethell and Mullee (1990) was reflected in the reduction in clinical angina compared with the patients of the control group. Also, 22 coronary artery disease patients participated in an experimental group that undertook a low fat vegetarian diet, stopped smoking, had stress management training and also participated in a moderate aerobic exercise program, reported a 91% reduction in the frequency of angina, a 42% reduction in duration of

angina and a 28% reduction in the severity of angina (Ornish *et al.*, 1990). In contrast, the 19 patients who formed the control group in the same study reported a 165% rise in frequency, a 95% rise in duration and a 39% rise in the severity of angina (Ornish *et al.*, 1990).

Loss of functional myocardium results in reduced left ventricular function, which can affect the patient's quality of life, and generally cause premature death (Boersma *et al.*, 2003). Damage to >12% of the myocardium increases two year mortality to 7% as compared to 0% for damage to <12% of the myocardium (Cerny & Burton, 2001). A myocardial infarction involving >35% of the left ventricle is predictive of a high short term mortality (Cerny & Burton, 2001). Therefore, the effect of physical training on survival depends on the patient's ejection fraction (Speecchia *et al.*, 1996). Among the 51 patients with ejection fraction <41%, the relative risk for the 27 untrained patients was 8.7 times higher than for the 24 trained ones (Speecchia *et al.*, 1996). When ejection fraction exceeded 40%, the estimated risk for an untrained patient was 1.07 times higher than for a trained person (Speecchia *et al.*, 1996).

In 15 acute myocardial infarction patients attending an early six week supervised aerobic exercise programme by circuit routine, the myocardial perfusion defect arising from an infarction was diminished in extent and severity (Gunning *et al.*, 2002). In patients who did not attend the same formal exercise programme this change was not observed (Gunning *et al.*, 2002). However, the number of the myocardial infarction patients studied was small but their study provided evidence to support the value of exercise training following myocardial infarction as a means of stimulating improved myocardial perfusion in the infarct zone (Gunning *et al.*, 2002).

It is likely that this improvement is facilitated by collateral development (Gunning *et al.*, 2002). Thus, the benefits of exercise are not only a consequence of peripheral physiological adaptation, but are a result of direct effects on myocardial perfusion (Gunning *et al.*, 2002). Therefore, a supervised exercise programme should be included in the standard rehabilitation protocol for patients recuperating after myocardial infarction (Gunning *et al.*, 2002).

Cardiovascular rehabilitation programmes significantly reduce mortality and percentage of complications, especially revascularization, unstable angina and heart failure (Maroto Montero *et al.*, 2005). Modification of lifestyle behaviours such as smoking, eating abundant quantities of fats, sedentary habits and methods of dealing with stress can significantly reduce risk of coronary heart disease (Maroto Montero *et al.*, 2005). The ten year follow-up results for morbidity showed a 63.15% incidence of control group patients with non fatal complication, which was much higher than that of the rehabilitation group (35.15%) (Maroto Montero *et al.*, 2005).

Physical activity is reputed to reduce depression and anxiety and to enhance mood in general. Exercise training alone or as a component of a multifactorial rehabilitation generally results in improvement in various measures of psychological status or functioning (Leon, 2000). Oldridge et al. (1990) compared two groups of myocardial infarction patients undergoing an exercise training programme and behavioural counselling or just community care. Subjects demonstrated moderate levels of depression or anxiety (Oldridge *et al.*, 1990). Results showed that an eight week aerobic exercise program reduced anxiety or depression (Oldridge *et al.*, 1990). Group counselling over eight weeks resulted in substantial reduction in depression

and promoted health related quality of life (Oldridge *et al.*, 1990). A few years later, Taylor (1997) randomised 54 myocardial infarction patients into three groups, an aerobic exercise training program and weekly discussion and information sessions group, a discussion and information only group and a control group. Only one group underwent an individually prescribed aerobic training program for six weeks, three times per week for 30 minutes (Taylor, 1997). A decrease in anxiety and depression rates was demonstrated for the three groups as well but the aerobic exercise training group demonstrated the largest decrease in scores of depression and the control group the least decrease (Taylor, 1997). However, exercise training alone does not appear to consistently result in improvement in measures of anxiety and depression (Leon, 2000).

5. Discussion

Complications of coronary heart disease are a leading cause of mortality worldwide (Moore, 2003). Although death rates from the disease have been falling since the early 1970s, coronary heart disease is still the most common cause of premature death in the United Kingdom (Moore, 2003). Each year 900,000 people in the United States of America experience acute myocardial infarction (Froelicher & Myers, 2006). Of these, roughly 225,000 die, including 125,000 who die before obtaining medical care (Froelicher & Myers, 2006). One in four men and one in six women die from coronary artery disease and in 2000, coronary heart disease caused around 125,000 deaths in the United Kingdom (Moore, 2003). Furthermore, illness and disability arising from coronary heart disease in older age groups is increasing (Moore, 2003).Thus, in addition to the human cost, coronary heart disease has major economic consequences (Moore, 2003). It is estimated that in the United Kingdom the combined coronary heart disease cost to the healthcare system and production losses from death and illness in those of working age represents a total of £ 10,000 million annually (Moore, 2003).

The overall benefits of cardiac rehabilitation are widely accepted. An exercise-based cardiovascular rehabilitation programme reduces both cardiac and total mortality but not the risk of recurrent myocardial infarction or revascularization. The trials reviewed assessed exercise therapy alone or in combination with educational and behavioural counselling and also across a range of exercise “doses”. The mechanisms behind the beneficial effects of exercise are not entirely clear but they probably include a decrease in atherogenesis or an improvement in the heart’s

ability to tolerate the consequences of ischaemia (Noble *et al.*, 2005). There is evidence that individuals who indulge in regular physical activity have a reduced incidence of myocardial infarction and reduced mortality from cardiovascular disease (Noble *et al.*, 2005) since it has been demonstrated to protect individuals from myocardial infarction or any other cardiovascular disease (Squires, 1998). More recent developments have shown that exercise training has direct benefits on the heart and the coronary vasculature, including myocardial oxygen demands, endothelial function, autonomic tone, coagulation and clotting factors, inflammatory markers and the development of coronary collateral vessels (Hambrecht *et al.*, 2000).However, coronary patients are heterogeneous groups and do not always demonstrate a predictable and consistent response to exercise training (Squires, 1998).

The importance of changing lifestyle to reduce the risk of further coronary artery disease events has been confirmed by several studies (Carlsson, 1998). Lifestyle factors refer to those risk factors which at least to some degree can be affected by the patients themselves (Carlsson, 1998). Examples are smoking, sedentary lifestyle and food habits (Carlsson, 1998). There is a trend to lower mortality and morbidity in patients who are physically more active but no study allows the researchers to make any definite conclusions about the effect of physical exercise itself in cardiac rehabilitation programs (Carlsson, 1998). Still, no secondary prevention study has confirmed a significant reduction of cardiac events from physical activity in patients with already established coronary vessel disease (Carlsson, 1998).

Not all of the trials provided fully details of the process of randomisation, allocation concealment or blinding of outcome assessment. As expected, the quality of the studies which were associated with greater reductions in all cause mortality was of a medium. Furthermore, the quality of trials did not appear to have improved over the last decades. Trails conducted though in the last decade have continued to report benefits of exercise-based cardiovascular programmes.

In patients with established coronary artery disease, exercise is associated with improved activity tolerance, modification of risk factors and improvement in quality of life (Gassner, Dunn & Piller, 2003). Regular exercise reduces the risk of overall mortality and cardiovascular mortality (Gassner, Dunn & Piller, 2003). It has been shown to prevent or delay future coronary deaths in patients with coronary artery disease (Gassner, Dunn & Piller, 2003). For example, a meta-analysis of 22 randomised trials of exercise based rehabilitation programs after myocardial infarction in 4554 patients was published in 1989 (O'Connor *et al.*, 1989). They found a 20% reduction for cardiovascular mortality and a 25% reduction in the risk for fatal reinfarction (O'Connor *et al.*, 1989). Similarly, Oldridge et al. (1988) performed a meta-analysis of ten trials including 4347 patients. They found a similar reduction for all-cause death and cardiovascular death in the patients undergoing cardiac rehabilitation (Oldridge *et al.*, 1988). They showed that comprehensive rehabilitation had a beneficial effect on mortality but unfortunately not on the rate of recurrent myocardial infarction incidents (Oldridge *et al.*, 1988).

A more recent systematic review of electronic databases from the earliest date available to December, 31st 1998 by Jolliffe and colleagues (2001) provided an

expanded meta-analysis of 8440 patients. They concluded that exercise based rehabilitation is effective in reducing cardiac deaths (Jolliffe *et al.*, 2001). They also reported that the population studied in their review was predominantly male, middle aged and low risk (Jolliffe *et al.*, 2001). Recently, Taylor et al. (2004) performed an updated meta-analysis of rehabilitation trials among patients with coronary heart disease. A total of 48 trials met their inclusion criteria including 8940 patients (Taylor *et al.*, 2004). Compared to usual care, cardiac rehabilitation was associated with reduced all-cause mortality and cardiovascular mortality (Taylor *et al.*, 2004). In addition, participation in the cardiac rehabilitation program was associated with greater reduction in cholesterol, triglycerides and systolic blood pressure (Taylor *et al.*, 2004). However, there were no differences between the rehabilitation and usual care groups in non fatal reinfarction or revascularization rates (Taylor *et al.*, 2004).

In general, cardiac rehabilitation programs offer education about the heart, the causes of the myocardial infarction incident and the risk factors for coronary artery disease (Carlsson, 1998). Cardiovascular rehabilitation programmes with aerobic exercise training for patients after an acute myocardial infarction incident improve exercise capacity, reduce coronary risk factors, improve the quality of life, reduce subsequent hospitalization costs and reduce major coronary artery disease events including fatal myocardial infarction, sudden death and all cause mortality (O' Connor *et al.*, 1989). These programs also address diet, emotional state, medicine and smoking cessation issues, but exercise training may be the most important part of these programs (Thompson, 2005). Indeed, in one meta-analysis of cardiac rehabilitation by O'Connor and colleagues (1989) there was no difference in cardiovascular outcomes between the exercise-only studies and those that included

other hygienic interventions attesting to the value of the exercise component (Thompson, 2005).

Cardiac rehabilitation programs may be based in hospitals or community centers or even at home. In recent years, structured home exercise programmes, with or without intermittent trans-telephonic electrocardiogram monitoring, have been shown to be feasible, safe and effective in increasing functional capacity especially in low risk patients after a myocardial infarction incident (DeBusk *et al.*, 1986). Nowadays, these home-based exercise programs are an attractive option in the present climate and offer advantages to patients in terms of convenience, abolition of travelling costs and the opportunity to become independent and responsible for regaining their own fitness at their own pace. Cardiac rehabilitation is now established as part of the cardiac care in the United Kingdom and is embedded in many government policies and national guidelines with structured exercise as a key element (Thow, 2006). Over the last ten years there has been a radical shift in the provision of exercise-based cardiac rehabilitation in the United Kingdom (Thow, 2006). Government recommendations and national guidelines encompass the traditional post myocardial infarction and revascularization groups, but also the older patient and the more complex cardiac groups, including those with heart failure and angina pectoris (Thow, 2006).

Although traditional exercise-based cardiac rehabilitation programs were designed for patients following a myocardial infarction, such programs are also being advocated for patients with stable angina pectoris, silent myocardial ischemia, following coronary artery bypass graft surgery, angioplasty of heart transplant and

for patients with stable heart failure with moderate to severe left ventricular systolic dysfunction (U.S. Department of Health and Human Services, 1995 as cited by Leon, 2000). Moreover, similar programs also have proven useful for patients with chronic pulmonary disease, peripheral vascular disease and diabetes mellitus (Leon, 2000).

The major limitation in performing these systematic reviews will be the availability of data on subjects and minority populations. Women typically comprise 20% to 30% of participants in randomised controlled trials, but risk estimates for women are infrequently published. Female individuals and the elderly are under-represented in exercise-based rehabilitation programs despite evidence suggesting that they achieve similar and possibly better physiological outcomes than younger male patients. In particular, research needs to address the reasons for non participation among the elderly and women and reasons for their lower referral rates. Therefore, more research is needed to determine how to increase rates of referral and adherence to exercise programmes. As it seems, motivation to an adequate level of physical activity will remain a major challenge and is open to future research.

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Table 5. Jadad scale for the potentially included randomised controlled trials

Study	Was the study described as randomised?	Was the study described as double blinded?	Was there a description of withdrawals and dropouts?	Was the randomization described as appropriate?	Was the blindness described as appropriate?	Total Jadad score
Ades et al., 1999	0	0	1	0	0	1/5
Amundsen et al., 2008	1	0	1	1	0	3/5
Bethell & Mullee, 1990	1	0	1	1	0	3/5
Carlsson, 1998	1	0	1	1	0	3/5
Dugmore et al., 1999	1	0	1	1	0	3/5
Eto et al., 2004	1	0	1	1	0	3/5
Giallauria et al., 2006	0	0	1	0	0	1/5
Gunning et al., 2002	1	0	1	1	0	3/5
Hambrecht et al., 2000	1	0	1	1	0	3/5
Hedbäck, Perk & Wodlin, 1993	0	0	1	0	0	1/5
Izawa et al., 2006	1	0	1	1	0	3/5
Lavie & Milani, 1996	0	0	1	0	0	1/5
Lee et al., 2008	1	0	1	1	0	3/5

Table 5. Continued

Study	Was the study described as randomised?	Was the study described as double blinded?	Was there a description of withdrawals and dropouts?	Was the randomization described as appropriate?	Was the blindness described as appropriate?	Total Jadad score
Leizorovicz et al., 1991	1	0	1	1	0	3/5
Malfatto et al., 1996	0	0	1	0	0	1/5
Marchionni et al., 2003	1	1	1	1	1	5/5
Maroto Montero et al., 2005	1	0	1	1	0	3/5
Motohiro et al., 2005	0	0	1	0	0	1/5
Oldridge et al., 1990	1	0	1	1	0	3/5
Ornish et al., 1990	1	0	1	1	0	3/5
Speecchia et al., 1996	1	0	1	1	0	3/5
Stähle et al., 1999	1	0	1	1	0	3/5
Taylor, 1997	1	0	1	1	0	3/5
Tsoukas, Andonakoudis & Christakos, 1995	1	0	1	1	0	3/5
Ueshima et al., 2005	0	0	1	0	0	1/5
Vona et al., 2004	1	1	1	1	1	5/5

Table 5. Continued

Study	Was the study described as randomised?	Was the study described as double blinded?	Was there a description of withdrawals and dropouts?	Was the randomization described as appropriate?	Was the blindness described as appropriate?	Total Jadad score
Walsh et al., 2003	0	0	1	0	0	1/5
Willmer et al., 1999	0	0	1	0	0	1/5
Witt et al., 2004	0	0	1	0	0	1/5
Yu et al., 2004	1	0	1	1	0	3/5

Amundsen et al. (2008)

PAPER SECTION **And topic**	**Item**	**Descriptor**	**Reported on Page #**
TITLE & ABSTRACT	1	How participants were allocated to interventions (*e.g.*, "random allocation", "randomised", or "randomly assigned").	The patients were randomised to either high or moderate intensity exercise group.
INTRODUCTION Background	2	Scientific background and explanation of rationale.	Peak oxygen consumption (VO_2peak) is a strong predictor of survival both in health subjects and patients with coronary heart disease. In patients with coronary artery disease, aerobic exercise training increases VO_2peak and reduces cardiovascular and total mortality
METHODS Participants	3	Eligibility criteria for participants and the settings and locations where the data were collected.	Patients were recruited to the study after coronary artery disease had been documented in at least one major epicardial artery during routine coronary angiography. The study was conducted in accordance with the Declaration of Helsinki and was approved by the Regional Medical Research Ethics Committee. Written informed consent was obtained from all patients.
Interventions	4	Precise details of the interventions intended for each group and how and when they were actually administered.	Training was done as uphill treadmill walking. After a five minute warm-up period at an intensity of 50-60% of VO_2peak (65-75% of HRpeak), the high intensity group completed 4 x 4 min intervals at 80-90% of VO_2peak (85-95% of HRpeak) separated by 3 minute pauses at 50-60% of VO_2peak. Each session ended with a five minute cool down walk at 50-60% of VO_2 peak. The moderate intensity group walked at 50-60% of VO_2 peak for 41 min, which equated the total O_2–uptake per session in the two groups.
Objectives	5	Specific objectives and hypotheses.	To study the effect of aerobic treadmill exercise training with different intensity on left ventricular function in patients with stable coronary artery disease, using Strain Rate- and Tissue Doppler Imaging.
Outcomes	6	Clearly defined primary and secondary outcome measures and, when applicable, any methods used to enhance the quality of measurements (*e.g.*, multiple	Even though the increase of VO_2 peak after training has been related to increased arteriovenous oxygen difference, previous studies have reported that cardiac adaptations and

		observations, training of assessors).	consequently cardiac output are the major determinants of VO_2 peak. In addition, cardiac output has been found to increase after training in coronary artery disease.
Sample size	7	How sample size was determined and, when applicable, explanation of any interim analyses and stopping rules.	17 patients were recruited to the study after coronary artery disease had been documented in at least one major epicardial artery during routine coronary angiography. Exclusion criteria were: left main coronary artery disease, unstable angina pectoris, intermittent claudication, myocardial infarction with the last 3 months, coronary artery disease bypass grafting or percutaneous coronary intervention performed within the last 12 months, complex ventricular arrhythmia, left ventricular ejection fraction during angiography <40%, orthopaedic or neurological limitations to exercise regular exercise during the last 3 months and failure to complete >70% of exercise sessions. No changes in medication were made during the study period.
Randomization -- Sequence generation	8	Method used to generate the random allocation sequence, including details of any restrictions (*e.g.*, blocking, stratification)	The patients were randomised by a computer random number generator to select random permuted blocks.
Randomization -- Allocation concealment	9	Method used to implement the random allocation sequence (*e.g.*, numbered containers or central telephone), clarifying whether the sequence was concealed until interventions were assigned.	---
Randomization -- Implementation	10	Who generated the allocation sequence, who enrolled participants, and who assigned participants to their groups.	Allocation, sequence and enrolment were performed by the authors involved in the present investigation.
Blinding (masking)	11	Whether or not participants, those administering the interventions, and those assessing the outcomes were blinded to group assignment. If done, how the success of blinding was evaluated.	No information regarding blinding was mentioned.
Statistical methods	12	Statistical methods used to compare groups for primary outcome(s); Methods for additional analyses, such as subgroup analyses and adjusted analyses.	Wilcoxon signed rank test was used to compare pre and post-test values within groups, and differences in change score between groups were evaluated by Mann Whitney U-test. Data are reported as median (range) if not specified otherwise. Spearman's rank coefficient was used for correlation analysis.

			A two tailed p<0.05 was considered statistically significant. Intra-observer variability of strain and SR measurements was calculated as the coefficient of repeatability and coefficient of variation
RESULTS Participant flow	13	Flow of participants through each stage (a diagram is strongly recommended). Specifically, for each group report the numbers of participants randomly assigned, receiving intended treatment, completing the study protocol, and analyzed for the primary outcome. Describe protocol deviations from study as planned, together with reasons.	A flow chart was not available
Recruitment	14	Dates defining the periods of recruitment and follow-up.	This article does not show the enrolment periods
Baseline data	15	Baseline demographic and clinical characteristics of each group.	All demographic data and baseline characteristics for the 17 post myocardial patients were reported in table 1.
Numbers analyzed	16	Number of participants (denominator) in each group included in each analysis and whether the analysis was by "intention-to-treat". State the results in absolute numbers when feasible (*e.g.*, 10/20, not 50%).	Of 21 patients who were recruited to the study after coronary artery disease had been documented in at least one major epicardial artery during routine coronary angiography. One patient withdrew due to lack of motivation, two due to physical impairment unrelated to cardiovascular disease, and one was excluded due to insufficient attendance to training sessions.
Outcomes and estimation	17	For each primary and secondary outcome, a summary of results for each group, and the estimated effect size and its precision (*e.g.*, 95% confidence interval).	The increase of VO_2peak was significantly higher (p<0.01) in the high intensity group (17 vs.8%). Mean LV early diastolic strain rate increased in the high, but not in the moderate, intensity group.
Ancillary analyses	18	Address multiplicity by reporting any other analyses performed, including subgroup analyses and adjusted analyses, indicating those pre-specified and those exploratory.	---
Adverse events	19	All important adverse events or side effects in each intervention group.	The study was powered to detect differences between the groups in VO_2peak, and the small number of patients increases the possibility of type-2 errors. The relatively low number of patients taking ACE inhibitors (35%) and beta-blockers (41%) was caused by the fact that only half the patients had sustained a MI and the occurrence of side-effects. No interventions (stenting or medical) that could have reduced

			the amount of ischemia and affected the results were made during the study period.
DISCUSSION Interpretation	20	Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision and the dangers associated with multiplicity of analyses and outcomes.	High-intensity aerobic exercise leads to larger improvements of VO_2peak compared to moderate intensity aerobic exercise training.
Generalizability	21	Generalizability (external validity) of the trial findings.	Aerobic treadmill exercise training with high, but not moderate, intensity improves left ventricular early diastolic myocardial relaxation rate in patients with stable coronary artery disease, and is also superior to moderate intensity exercise for improving VO_2peak.
Overall evidence	22	General interpretation of the results in the context of current evidence.	The present study shows that high, but not moderate, intensity aerobic exercise training improves early diastolic myocardial relaxation rate in patients with coronary artery disease.

Bethell & Mullee (1990)

PAPER SECTION **And topic**	**Item**	**Descriptor**	**Reported on Page #**
TITLE & ABSTRACT	1	How participants were allocated to interventions (*e.g.*, "random allocation", "randomised", or "randomly assigned").	The patients were either randomised to either a treatment group or a control group.
INTRODUCTION Background	2	Scientific background and explanation of rationale.	The benefits of exercise training for patients with coronary heart disease are widely recognized. Numerous studies have shown these effects and the mechanism of their production in selected groups of patients.
METHODS Participants	3	Eligibility criteria for participants and the settings and locations where the data were collected.	All male patients aged 65 or less admitted to Basingstoke District Hospital with a provisional diagnosis of acute myocardial infarction were recruited to the study.
Interventions	4	Precise details of the interventions intended for each group and how and when they were actually administered.	The exercises were performed as eight stages on a circuit: bicycling on an ergometer, stepping up and down two steps, as overhead pull of 20kg, a squat lift against 40kg, a bench press against 10-20kg and sitting leg press against 50kg. The weight training exercises were performed on a Nissen polygym and involve frequent rapid repetitions with small loads, they are dynamic not like weight lifting which is nearly isometric. At the start of the course the patient cycled on the ergometer at 50W for 15 seconds and repeated each exercise five times. The number of repetitions and the number of circuits were built up gradually depending on his pulse rate response at the previous session. The aim was to exercise him to between 70% and 85% of his predicted maximum heart rate. The whole session lasted between 20 and 30 minutes.
Objectives	5	Specific objectives and hypotheses.	To assess the results of managing patients after myocardial infarction
Outcomes	6	Clearly defined primary and secondary outcome measures and, when applicable, any methods used to enhance the quality of measurements (*e.g.*, multiple observations, training of assessors).	There have, however, been very few large scale randomised controlled trials in unselected patients recovering from acute myocardial infarction and only one in the United Kingdom-and that was hospital-based.
Sample size	7	How sample size was determined and, when	A chest x ray was taken within 48 hours of admission. By the

		applicable, explanation of any interim analyses and stopping rules.	5th day of admission a positive diagnosis of acute myocardial infarction was made only if all of the following criteria were met: a history of chest pain typical of myocardial infarction, progressive electrocardiogram changes, and a rise and fall in aspartate transaminase concentrations with at least one reading above 40 units/ml. Patients were excluded if they lived more that 25 miles from Alton, if they had medical or orthopaedic problems that precluded their taking part in the exercise course, if they had insulin dependent diabetes mellitus or were in atrial fibrillation, if they had previously been through the course of if they were on the investigator's personal general practice list.
Randomization -- Sequence generation	8	Method used to generate the random allocation sequence, including details of any restrictions (*e.g.*, blocking, stratification)	The qualifying patients were randomised by order of admission into treatment and control groups by means of a random letter sequence.
Randomization -- Allocation concealment	9	Method used to implement the random allocation sequence (*e.g.*, numbered containers or central telephone), clarifying whether the sequence was concealed until interventions were assigned.	---
Randomization -- Implementation	10	Who generated the allocation sequence, who enrolled participants, and who assigned participants to their groups.	Allocation, sequence and enrolment were performed by the authors involved in the present investigation.
Blinding (masking)	11	Whether or not participants, those administering the interventions, and those assessing the outcomes were blinded to group assignment. If done, how the success of blinding was evaluated.	No information regarding blinding was mentioned.
Statistical methods	12	Statistical methods used to compare groups for primary outcome(s); Methods for additional analyses, such as subgroup analyses and adjusted analyses.	Mann-Whitney U tests and two-sample *t* tests were used to test for differences between the two groups (controls and treated) and Wilcoxon-signed-rank tests or paired *t* tests were used to test for differences within the two groups. Chi-squared test with Yates's correction factor and McNemar's test were also used when appropriate. Ninety five per cent confidence intervals for x^3 tests were calculated according to the method described by Armitage and Berry. Most of the statistical analyses were computed with the statistical packages SPSS-X

			and Minitab.
RESULTS Participant flow	13	Flow of participants through each stage (a diagram is strongly recommended). Specifically, for each group report the numbers of participants randomly assigned, receiving intended treatment, completing the study protocol, and analyzed for the primary outcome. Describe protocol deviations from study as planned, together with reasons.	A flow chart was available.
Recruitment	14	Dates defining the periods of recruitment and follow-up.	Patients who were admitted to the Basingstoke District Hospital Coronary Care Unite between 1 December 1979 and 1 March 1984
Baseline data	15	Baseline demographic and clinical characteristics of each group.	The baseline demographic and clinical characteristics are not mentioned
Numbers analyzed	16	Number of participants (denominator) in each group included in each analysis and whether the analysis was by "intention-to-treat". State the results in absolute numbers when feasible (*e.g.*, 10/20, not 50%).	Of the 331 patients who were admitted with a confirmed diagnosis of acute myocardial infarction, 28 died before randomization and 54 were excluded. The remaining 229 were randomised- 113 to the treatment group and 116 to the control group. Of the 113 treatment patients, 99 attended Alton Sports Centre for the 1st exercise test (5 died, 4 refused and 5 developed other problems). Of the 116 control patients, 101 attended Alton Sports Centre (7 died, 3 refused and 5 developed other problems).
Outcomes and estimation	17	For each primary and secondary outcome, a summary of results for each group, and the estimated effect size and its precision (*e.g.*, 95% confidence interval).	There were no significant differences between the two groups for change in frequency of sexual intercourse, resting heart rate, and blood cholesterol or triglyceride concentration. The mean increase in weight of the treatment patients was significantly greater than in the control patients. The increase in the occurrence of angina in the control group was significant. The median energy level was significantly greater in the treatment group than in the controls. The mean difference in the increase of predicted maximum oxygen uptake was 2-35 ml/min/kg, which was significantly greater in the treatment group than in the control group. The decrease in the mean double product was significantly greater in the treatment group than in the control group.

Ancillary analyses	18	Address multiplicity by reporting any other analyses performed, including subgroup analyses and adjusted analyses, indicating those pre-specified and those exploratory.	---
Adverse events	19	All important adverse events or side effects in each intervention group.	Heart rate measurements were taken from an electrocardiographic write-out and should not have been subject to bias. However, it is possible that peak systolic blood pressures, read from an analogue electronic sphygmomanometer, were subject to observer bias. A standardized questionnaire for the determination of angina was not used and the findings of this symptom may have been biased.
DISCUSSION Interpretation	20	Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision and the dangers associated with multiplicity of analyses and outcomes.	The benefits of an exercise-based cardiovascular rehabilitation program were well manifested.
Generalizability	21	Generalizability (external validity) of the trial findings.	This study showed the feasibility, the safety, and the benefits of a community based exercise programme supervised by a general practitioner for patients recovering from acute myocardial infarction. Every district general hospital should be able to offer this treatment to patients after myocardial infarction and those after coronary bypass graft but most do not. The community programme is one of the ways in which the gaps in the present provision could be filled.
Overall evidence	22	General interpretation of the results in the context of current evidence.	This trial attempted to assess the effects of a community based exercise programme and it showed that most patients can participate (85% of patients who lived within 25 miles of the sports centre took part).

Carlsson (1998)

PAPER SECTION **And topic**	**Item**	**Descriptor**	**Reported on Page #**
TITLE & ABSTRACT	1	How participants were allocated to interventions (*e.g.*, "random allocation", "randomised", or "randomly assigned").	The patients were randomised either to the intervention group or the control group.
INTRODUCTION Background	2	Scientific background and explanation of rationale.	In Sweden there is a gradient with increasing morbidity and mortality in CAD from the south to the north and from the east to the west. In Sweden CAD deaths accounts for more than 50% of all death, 30% of all in-patient care days and 10% of all early retirements
METHODS Participants	3	Eligibility criteria for participants and the settings and locations where the data were collected.	All patients with a suspected myocardial infarction admitted to the hospital were hospitalized. All patients are transferred to the coronary care unit at Department of Internal Medicine in Malmo, Sweden, for further treatment. The study was approved by local Ethical Committee.
Interventions	4	Precise details of the interventions intended for each group and how and when they were actually administered.	After randomisation, patients in the intervention groups were invited to participate in a continuous physical exercise programme 2–3 times weekly for a period of 2–3 months. The exercise sessions lasted one hour and were comprised of the following parts: 10 minutes of warm-up, 40 minutes of interval walking or jogging, 10 minute cool down period (consisting of relaxation and light stretching exercises) Individual exercise schedules were provided to the patients in the intervention groups in order to maintain the effects of the exercise programme beyond the discharge from the hospital training centre.
Objectives	5	Specific objectives and hypotheses.	To evaluate the one-year effect of a secondary prevention programme on the work capacity of patients recovering from an acute myocardial infarction or coronary artery bypass surgery, as compared to that of patients referred to their primary care physician.
Outcomes	6	Clearly defined primary and secondary outcome measures and, when applicable, any methods used to	Several trials have been conducted by randomizing patients with myocardial infarction either to physical exercise programs

		enhance the quality of measurements (*e.g.*, multiple observations, training of assessors).	or to control groups. There is a trend to lower mortality and morbidity in patients who are physically more active but no study allows to make any definite conclusions about the effect of physical exercise itself in cardiac rehabilitation.
Sample size	7	How sample size was determined and, when applicable, explanation of any interim analyses and stopping rules.	121 AMI patients and 56 CABG patients were eligible for evaluation. Patients were excluded from randomisation if any of the following criteria were present: signs of unstable angina, i.e. new chest pain at rest or worsening of the angina, signs of ST-depression at the exercise test of more than 3 mm in two chest leads or more than 2 mm in two limb leads at four weeks post discharge from hospital, signs of congestive heart failure, severe non-cardiac disease, drinking problems, if not Swedish spoken and if unwilling to participate.
Randomization -- Sequence generation	8	Method used to generate the random allocation sequence, including details of any restrictions (*e.g.*, blocking, stratification)	Patients were randomly allocated to the intervention or the reference group and randomisation was made in groups of 20.
Randomization -- Allocation concealment	9	Method used to implement the random allocation sequence (*e.g.*, numbered containers or central telephone), clarifying whether the sequence was concealed until interventions were assigned.	---
Randomization -- Implementation	10	Who generated the allocation sequence, who enrolled participants, and who assigned participants to their groups.	Allocation, sequence and enrolment were performed by the authors involved in the present investigation.
Blinding (masking)	11	Whether or not participants, those administering the interventions, and those assessing the outcomes were blinded to group assignment. If done, how the success of blinding was evaluated.	No information regarding blinding was mentioned.
Statistical methods	12	Statistical methods used to compare groups for primary outcome(s); Methods for additional analyses, such as subgroup analyses and adjusted analyses.	The data were analysed by cross tabulation, independent samples *t*-test for inter-group analysis and paired samples *t*-test for intra-group analysis. Statistical significance was assumed at $P < 0.05$. All tests were two-tailed.

RESULTS Participant flow	13	Flow of participants through each stage (a diagram is strongly recommended). Specifically, for each group report the numbers of participants randomly assigned, receiving intended treatment, completing the study protocol, and analyzed for the primary outcome. Describe protocol deviations from study as planned, together with reasons.	A flow chart was not available.
Recruitment	14	Dates defining the periods of recruitment and follow-up.	This article does not show the enrolment periods
Baseline data	15	Baseline demographic and clinical characteristics of each group.	All demographic data and baseline characteristics for the post myocardial and CABG patients were reported in table X.
Numbers analyzed	16	Number of participants (denominator) in each group included in each analysis and whether the analysis was by "intention-to-treat". State the results in absolute numbers when feasible (*e.g.*, 10/20, not 50%).	Of the total of 268 patients, 32 patients who met the eligibility criteria were excluded from randomisation (8 patients with severe non-cardiac disease, 3 with drinking problems, 2 which were non-Swedish speaking, 19 who refused to participate). In addition, 68 AMI patients were excluded from randomisation for clinical reasons. 2 AMI patients randomised to the intervention group and 2 randomised to the reference group died. 43 patients were excluded post randomisation because of a lack of data on the exercise test results. Thus, at the end of the follow-up time, 121 AMI patients, 61 randomised to the AMI intervention group and 60 to the AMI reference group, were eligible for evaluation. Of a total of 76 CABG patients, 10 were excluded from randomisation (9 patients were unwilling to participate and 1 was non-Swedish speaking).9 were excluded for clinical reasons. 1 patient randomised to the intervention group interrupted the follow-up programme. Thus, 56 CABG patients, 27 in the CABG intervention group and 29 in the CABG reference group, were eligible for evaluation.
Outcomes and estimation	17	For each primary and secondary outcome, a summary of results for each group, and the estimated effect size and its precision (*e.g.*, 95% confidence interval).	Patients in all groups, except patients in the AMI reference group, increased their work capacity significantly.
Ancillary analyses	18	Address multiplicity by reporting any other analyses performed, including subgroup analyses and adjusted analyses, indicating those pre-specified and those exploratory.	---

Adverse events	19	All important adverse events or side effects in each intervention group.	When tested with a paired sample *t*-test, work load capacity increased significantly within the AMI intervention group. However, when compared to the change in the AMI reference group, using independent sample *t*-test, the changes did not differ significantly. Thus, we cannot state that the exercise intervention had any effect on work load capacity in AMI patients.
DISCUSSION Interpretation	20	Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision and the dangers associated with multiplicity of analyses and outcomes.	Training programs consisting of three months of exercise training within the hospital and with recommendations of further exercise is not enough to maintain a training effect.
Generalizability	21	Generalizability (external validity) of the trial findings.	The present secondary prevention program with a structured follow-up model including patients with CAD have shown that it takes more than three months of physical training in combination with nurse counselling to maintain improved attitudes to physical exercise.
Overall evidence	22	General interpretation of the results in the context of current evidence.	Training programs must be organised in another way like long term training in groups outside the hospital. Psychological aspects of quality of life are important in secondary prevention. Quality of life is considerably affected, especially during the initial recovery phase after a cardiac event.

Dugmore et al. (1999)

PAPER SECTION **And topic**	**Item**	**Descriptor**	Reported on Page #
TITLE & ABSTRACT	1	How participants were allocated to interventions (e.g., "random allocation", "randomised", or "randomly assigned").	Patients were randomly allocated to a regular weekly aerobic training programme or a control group.
INTRODUCTION Background	2	Scientific background and explanation of rationale.	There are conflicting opinions in the United Kingdom over the value and benefit of cardiac rehabilitation. Some protagonists firmly believe that it has a positive effect on the recovery process following myocardial infarction. Others have questioned this and have claimed that while exercise training in particular increases confidence during the early stages of convalescence after myocardial infarction, in the long term it has little effect on cardiac function, everyday life, and emotional state. This has led to suggestions that formal exercise programmes are probably not justified for all patients.
METHODS Participants	3	Eligibility criteria for participants and the settings and locations where the data were collected.	Patients recruited for this study were drawn from the clinical workload of the consultant physicians at Russells Hall Hospital, Dudley, West Midlands, UK. The research population included 124 patients (122 male and 2 female) who had all suffered clinically documented myocardial infarction.
Interventions	4	Precise details of the interventions intended for each group and how and when they were actually administered.	Patients in both good and poor prognosis treatment groups received regular aerobic and local muscular endurance training three times a week for a 12 month period. This consisted of warm up and cool down exercises, sit ups, wall bar/bench step ups, cycle ergometer, and a major component centred on the training of aerobic capacity, using walking and jogging. Each patient's training programme was individually designed and based on the results of regular exercise tests and trial exercise prescriptions. Individual training intensities varied between approximately 50–65% of measured peak oxygen uptake in the poor prognosis patients and 65–80% of peak oxygen consumption in those with a good prognosis. In addition, each patient rated their "perceived exertion" in response to every

			training session using the Borg scale.
Objectives	5	Specific objectives and hypotheses.	To examine and evaluate improvements in cardiorespiratory fitness, psychological wellbeing, quality of life, and vocational status in post myocardial infarction patients during and after a comprehensive 12 month exercise rehabilitation programme.
Outcomes	6	Clearly defined primary and secondary outcome measures and, when applicable, any methods used to enhance the quality of measurements (*e.g.*, multiple observations, training of assessors).	Cardiac rehabilitation and specifically exercise training in patients after myocardial infarction may require labour intensive efforts to be effective. In order to justify its wider use with such populations, its physiological, psychosocial, and vocational benefits need to be critically examined. There have been no randomised controlled studies on these outcomes in the United Kingdom, although it has been suggested that cardiac rehabilitation is an efficient use of health care resources.
Sample size	7	How sample size was determined and, when applicable, explanation of any interim analyses and stopping rules.	Patients were classified as having either a good or a poor prognosis on the basis of their initial responses to early exercise testing. The criteria used to determine prognosis included: degree of ST segment depression (> 2 mm for classification into the poor prognosis group), heart rate response to exercise uncontrolled by medication (> 130 beats/min for classification into the poor prognosis group), number and classification of ventricular premature beats (rated 3 to 5 on the Lown classification), exercise time (considerably less than nine minutes for classification into the poor prognosis group), symptoms of chest discomfort and/or dyspnoea (of sufficient intensity to require stopping the test, resulting in classification into the poor prognosis group). A minimum of at least three negative responses was necessary for final classification into the poor prognosis group.
Randomization -- Sequence generation	8	Method used to generate the random allocation sequence, including details of any restrictions (*e.g.*, blocking, stratification)	Random assignment with no more details was used to allocate participants to either training or no training group.
Randomization -- Allocation	9	Method used to implement the random allocation sequence (*e.g.*, numbered containers or central	---

concealment		telephone), clarifying whether the sequence was concealed until interventions were assigned.	
Randomization -- Implementation	10	Who generated the allocation sequence, who enrolled participants, and who assigned participants to their groups.	Allocation, sequence and enrolment were performed by the authors involved in the present investigation.
Blinding (masking)	11	Whether or not participants, those administering the interventions, and those assessing the outcomes were blinded to group assignment. If done, how the success of blinding was evaluated.	No information regarding blinding was mentioned.
Statistical methods	12	Statistical methods used to compare groups for primary outcome(s); Methods for additional analyses, such as subgroup analyses and adjusted analyses.	Standard parametric statistical techniques were used throughout. The mean and standard error of the mean (SEM) were calculated and used to describe and summarise the data. The standard deviation (SD) was used when appropriate to illustrate the dispersal of scores around the mean. The Student's *t* test was employed when testing the significance of the difference between two means using the appropriate test for matched or independent means. Analysis of variance was also used where applicable. Differences and relations were considered significant at the 5% level. Relations between two or more variables were evaluated using the Pearson product moment correlation coefficient. Correlation and regression methods were used to identify interrelations between variables and to measure average improvements over time.
RESULTS Participant flow	13	Flow of participants through each stage (a diagram is strongly recommended). Specifically, for each group report the numbers of participants randomly assigned, receiving intended treatment, completing the study protocol, and analyzed for the primary outcome. Describe protocol deviations from study as planned, together with reasons.	A flow chart was not available.
Recruitment	14	Dates defining the periods of recruitment and follow-up.	The recruitment of patients was between 1984 and 1988 and the follow-up lasted 5 years.
Baseline data	15	Baseline demographic and clinical characteristics of each group.	Further descriptive characteristics of these groups relevant to exercise rehabilitation are given in table 1.
Numbers	16	Number of participants (denominator) in each group	The population was subdivided into groups with good and bad

analyzed		included in each analysis and whether the analysis was by "intention-to-treat". State the results in absolute numbers when feasible (*e.g.*, 10/20, not 50%).	prognosis, based on criteria. *Good prognosis group*—There were 36 patients with a good prognosis and their matched controls. Of these, 19 pairs had had an anterior infarct and 17 pairs an inferior infarct. *Poor prognosis group*—There were 26 patients with a poor prognosis and their matched controls. Of these, 14 pairs had had an anterior infarct and 12 pairs an inferior infarct. 14 pairs from the good prognosis group and 3 pairs from the poor prognosis group were taking β-blockers.
Outcomes and estimation	17	For each primary and secondary outcome, a summary of results for each group, and the estimated effect size and its precision (*e.g.*, 95% confidence interval).	Differences in cardiorespiratory, psychological, and quality of life scores were compared between good and poor prognosis patients and their matched controls over 12 months. At the five year follow up the authors considered selected differences in vocational status and lifestyle changes when comparing the total exercising populations (good and poor prognosis combined) with their matched controls.
Ancillary analyses	18	Address multiplicity by reporting any other analyses performed, including subgroup analyses and adjusted analyses, indicating those pre-specified and those exploratory.	---
Adverse events	19	All important adverse events or side effects in each intervention group.	There were no cardiac arrests during the 12 month exercise training period.
DISCUSSION Interpretation	20	Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision and the dangers associated with multiplicity of analyses and outcomes.	Significant improvements in cardiorespiratory fitness, psychological profiles and quality of life scores were recorded in the treatment population when compared with their matched controls. Although there were no significant differences in mortality, a larger percentage of the regular exercisers resumed full time employment and they returned to work earlier than the controls. Controls took lighter jobs, lost more time from work, and suffered more non-fatal re-infarctions.
Generalizability	21	Generalizability (external validity) of the trial findings.	There have been few randomised controlled trials of exercise in the rehabilitation of post myocardial infarction populations in the United Kingdom. The early investigations gave the impetus for the wide acceptance of this type of management.
Overall evidence	22	General interpretation of the results in the context of current evidence.	Regularly supervised and prolonged aerobic exercise training improves cardiorespiratory fitness, psychological status, and

			quality of life. The trained population also had a reduction in morbidity following myocardial infarction, and significant improvement in vocational status over a five year follow up period.

Eto et al. (2004)

PAPER SECTION **And topic**	**Item**	**Descriptor**	**Reported on Page #**
TITLE & ABSTRACT	1	How participants were allocated to interventions (*e.g.*, "random allocation", "randomised", or "randomly assigned").	Patients were randomly assigned to either a training group or a control group 1 week after the onset of AMI.
INTRODUCTION Background	2	Scientific background and explanation of rationale.	End-tidal CO_2 partial pressure has been suggested as a non-invasive index reflecting cardiac output under constant ventilation. It has been suggested that exercise training improves the cardiac output response to exercise in patients with previous myocardial infarction, but individual evaluation has been limited partly because of the invasiveness and difficulties inherent in the method used to measure cardiac output. If the response of cardiac output during exercise could be estimated noninvasively, it would be of practical use in evaluating the therapeutic effects of training in patients with various heart diseases.
METHODS Participants	3	Eligibility criteria for participants and the settings and locations where the data were collected.	Patients with pulmonary congestion, dyspnoea at rest, serious arrhythmia, left ventricular aneurysm, valvular lesions or primary lung disease were excluded. All patients were hospitalized and conventional medications were prescribed during the study period. The Ethics Committee of the Cardiovascular Institute approved the study protocol and informed consent was obtained from all patients.
Interventions	4	Precise details of the interventions intended for each group and how and when they were actually administered.	The training group then started 30min of supervised bicycle exercise with a constant workload at the anaerobic threshold level, twice daily for 1 week. After the first week of training, the exercise intensity was increased to a new anaerobic threshold level that was determined at the second exercise testing. Meanwhile, the control group performed walking exercise according to the conventional rehabilitation protocol. They started walking 200m along a corridor in the hospital 3 times a day, 1 week after the onset of AMI. The walking distance was gradually increased up to

			500m by the end of the study period.
Objectives	5	Specific objectives and hypotheses.	The aim of this study was to examine whether $PETCO_2$ does reflect cardiac output, even during exercise, in patients with acute myocardial infarction undergoing exercise training early after onset.
Outcomes	6	Clearly defined primary and secondary outcome measures and, when applicable, any methods used to enhance the quality of measurements (*e.g.*, multiple observations, training of assessors).	End-tidal CO_2 pressure ($PETCO_2$) is a non-invasive index obtained from respiratory gas monitoring. Variations in $PETCO_2$ have been shown to reflect changes in cardiac output and pulmonary blood flow in animals and humans under constant ventilation. It has been reported that $PETCO_2$ is influenced by changes of heart rate (presumably cardiac output) in patients with a pacemaker. Compared with normal subjects, patients with a pulmonary embolism have a low $PETCO_2$, probably because of increased physiological dead space attributable to decreased pulmonary blood flow. It has also been shown that patients with cardiac disease have an abnormally low $PETCO_2$ during exercise, especially those with an impaired response of cardiac output during exercise or with decreased peak oxygen uptake.
Sample size	7	How sample size was determined and, when applicable, explanation of any interim analyses and stopping rules.	Thirty-six patients (35 men, 1 woman) were randomly assigned to either a training group or a control group 1 week after the onset of AMI.
Randomization -- Sequence generation	8	Method used to generate the random allocation sequence, including details of any restrictions (*e.g.*, blocking, stratification)	Random assignment with no more details was used to allocate participants to either training or no training group.
Randomization -- Allocation concealment	9	Method used to implement the random allocation sequence (*e.g.*, numbered containers or central telephone), clarifying whether the sequence was concealed until interventions were assigned.	---
Randomization -- Implementation	10	Who generated the allocation sequence, who enrolled participants, and who assigned participants to their groups.	Allocation, sequence and enrolment were performed by the authors involved in the present investigation.
Blinding (masking)	11	Whether or not participants, those administering the interventions, and those assessing the outcomes were blinded to group assignment. If done, how the success	No blinding was mentioned

		of blinding was evaluated.	
Statistical methods	12	Statistical methods used to compare groups for primary outcome(s); Methods for additional analyses, such as subgroup analyses and adjusted analyses.	Data are expressed as means ± SD. Inter-group differences were compared by the unpaired t-test. The time course changes in ventilatory parameters were analyzed by analysis of variance for repeated measures followed by the Fisher's test. A p value <0.05 was considered significant.
RESULTS Participant flow	13	Flow of participants through each stage (a diagram is strongly recommended). Specifically, for each group report the numbers of participants randomly assigned, receiving intended treatment, completing the study protocol, and analyzed for the primary outcome. Describe protocol deviations from study as planned, together with reasons.	A flow chart was not available
Recruitment	14	Dates defining the periods of recruitment and follow-up.	This article does not show the enrolment periods
Baseline data	15	Baseline demographic and clinical characteristics of each group.	All demographic data and baseline characteristics were reported in table 1.
Numbers analyzed	16	Number of participants (denominator) in each group included in each analysis and whether the analysis was by "intention-to-treat". State the results in absolute numbers when feasible (*e.g.*, 10/20, not 50%).	The 13 patients (70 %) in the training group and 12 patients (67 %) in the control group underwent successful percutaneous coronary intervention before entering the study.
Outcomes and estimation	17	For each primary and secondary outcome, a summary of results for each group, and the estimated effect size and its precision (*e.g.*, 95% confidence interval).	Those in the training group performed exercise training under supervision at the anaerobic threshold level for 2 weeks, while patients in the control group followed a conventional walking regimen. In the training group, but not in the control group, $PETCO_2$ at the respiratory compensation point increased significantly. Similarly, the cardiac index at peak exercise increased only in the training group. Peak oxygen uptake and anaerobic threshold were increased only in the training group
Ancillary analyses	18	Address multiplicity by reporting any other analyses performed, including subgroup analyses and adjusted analyses, indicating those pre-specified and those exploratory.	---
Adverse events	19	All important adverse events or side effects in each intervention group.	No adverse event or side effects were mentioned.

DISCUSSION Interpretation	20	Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision and the dangers associated with multiplicity of analyses and outcomes.	Exercise training improves the cardiac output response to exercise in patients with previous myocardial infarction.
Generalizability	21	Generalizability (external validity) of the trial findings.	Aerobic exercise training started early after AMI increased $PETCO_2$ during exercise, and this increase was associated with an increase in the cardiac output. The increase in $PETCO_2$ probably reflects an improvement of the cardiac output during exercise in response to physical training via decreased ventilation –perfusion mismatch.
Overall evidence	22	General interpretation of the results in the context of current evidence.	The present study showed that the level of $PETCO_2$ during exercise was increased by physical training for 2 weeks in patients after AMI. The increase in $PETCO_2$ at the respiratory compensation point observed in the training group was associated with a greater increase in cardiac output at peak exercise.

Gunning et al. (2002)

PAPER SECTION **And topic**	**Item**	**Descriptor**	**Reported on Page #**
TITLE & ABSTRACT	1	How participants were allocated to interventions (*e.g.*, "random allocation", "randomised", or "randomly assigned").	Patients were randomised into a supervised exercise training programme and a control group.
INTRODUCTION Background	2	Scientific background and explanation of rationale.	Several studies have supported exercise training following myocardial infarction on the grounds that improved peripheral conditioning results in reduced cardiac work. Modification of weight, lipid profile and the concomitant alteration of risk factors such as smoking which accompany an active rehabilitation programme have all been shown to benefit the patient following an infarct.
METHODS Participants	3	Eligibility criteria for participants and the settings and locations where the data were collected.	Infarction was diagnosed according to standard ECG criteria (1-mm ST segment elevation in two contiguous inferior leads, 2-mm ST segment elevation in two contiguous chest leads, new left bundle branch block) accompanying a history of ischemic chest pain and subsequent elevation in serum creatine kinase. All received thrombolysis within 6 h of the onset of symptoms
Interventions	4	Precise details of the interventions intended for each group and how and when they were actually administered.	Patients who were randomised into the exercise arm of the study attended the department within 2 weeks of discharge and then twice weekly over a 6-week period. Following a 10-min warm-up period aerobic exercise was conducted by ergometer or circuit routine sustained over 20 min to maintain a target heart rate between 60% and 80% of the age-predicted maximum. A warm-down period of 10 min followed
Objectives	5	Specific objectives and hypotheses.	The effects of a 6-week exercise programme on the thallium-201 myocardial perfusion characteristics of patients following myocardial infarction were evaluated.
Outcomes	6	Clearly defined primary and secondary outcome measures and, when applicable, any methods used to enhance the quality of measurements (*e.g.*, multiple observations, training of assessors).	It has not been clearly shown that exercise training directly modifies myocardial perfusion after such an event.

Sample size	7	How sample size was determined and, when applicable, explanation of any interim analyses and stopping rules.	Twenty-five patients (23 male, median age 64 years, range 51–82) completed the protocol. Patients were to one of two groups: those undergoing a 6-week supervised exercise programme and those not undergoing an exercise programme.
Randomization -- Sequence generation	8	Method used to generate the random allocation sequence, including details of any restrictions (*e.g*., blocking, stratification)	Random assignment with no more details was used to allocate participants to either training or no training group.
Randomization -- Allocation concealment	9	Method used to implement the random allocation sequence (*e.g*., numbered containers or central telephone), clarifying whether the sequence was concealed until interventions were assigned.	---
Randomization -- Implementation	10	Who generated the allocation sequence, who enrolled participants, and who assigned participants to their groups.	Allocation, sequence and enrolment were performed by the authors involved in the present investigation.
Blinding (masking)	11	Whether or not participants, those administering the interventions, and those assessing the outcomes were blinded to group assignment. If done, how the success of blinding was evaluated.	No blinding was mentioned
Statistical methods	12	Statistical methods used to compare groups for primary outcome(s); Methods for additional analyses, such as subgroup analyses and adjusted analyses.	Summary data are expressed as mean with standard deviation. Mean values of defect extent, severity and percentage reversibility and hemodynamic parameters were compared using the Student's *t*-test. Results were considered significant where *P*= 0.05.
RESULTS Participant flow	13	Flow of participants through each stage (a diagram is strongly recommended). Specifically, for each group report the numbers of participants randomly assigned, receiving intended treatment, completing the study protocol, and analyzed for the primary outcome. Describe protocol deviations from study as planned, together with reasons.	A flow chart was not available
Recruitment	14	Dates defining the periods of recruitment and follow-up.	This article does not show the enrolment periods
Baseline data	15	Baseline demographic and clinical characteristics of each group.	All demographic data and baseline characteristics for the post myocardial patients were reported in table 1.
Numbers	16	Number of participants (denominator) in each group	Ten patients either failed to complete all 12 visits to the

analyzed		included in each analysis and whether the analysis was by "intention-to-treat". State the results in absolute numbers when feasible (*e.g.*, 10/20, not 50%).	exercise classes or declined follow-up thallium scans. These have not been entered into the analysis
Outcomes and estimation	17	For each primary and secondary outcome, a summary of results for each group, and the estimated effect size and its precision (*e.g.*, 95% confidence interval).	A total of 29 perfusion defects were identified, 18 in the exercise group and 11 in the control group. Over 3 months in the exercise group the mean extent of the stress image defect fell while in the control group there was an increase. Stress defect severity fell in the exercise group but increased in the control group. On redistribution imaging in the exercise group a significant decrease was observed in both extent and severity of the defects. However in the control group no significant change was observed for extent or severity of the redistribution defects. Reversibility of the defects increased slightly in both the exercise group and the control group.
Ancillary analyses	18	Address multiplicity by reporting any other analyses performed, including subgroup analyses and adjusted analyses, indicating those pre-specified and those exploratory.	----
Adverse events	19	All important adverse events or side effects in each intervention group.	The number of patients studied was small and the inability to include 10 patients contributed to this. In performing this study the aim was to assess objective perfusion characteristics only. Changes in left ventricular function and patient symptom status were not incorporated into the protocol. Such data may have enhanced our findings.
DISCUSSION Interpretation	20	Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision and the dangers associated with multiplicity of analyses and outcomes.	A supervised exercise programme should be included in the standard rehabilitation protocol for patients recuperating after myocardial infarction.
Generalizability	21	Generalizability (external validity) of the trial findings.	Our data provide evidence to support the value of exercise training following myocardial infarction as a means of stimulating improved myocardial perfusion in the infarct zone. It is likely that this improvement is facilitated by collateral development. Thus the benefits of exercise are not only a consequence of peripheral physiological adaptation, but are a result of direct effects on myocardial perfusion.

Overall evidence	22	General interpretation of the results in the context of current evidence.	Our results suggest that improvement in thallium defects in a3-month period reflect sufficient time for collaterals to improve following infarction in humans. In view of the reduction in the severity and extent of the redistribution thallium defects observed in the exercise group, but not the control group, formal exercise training appears to be a stimulus for such collateral recruitment.

Hambrecht et al. (2000)

PAPER SECTION **And topic**	**Item**	**Descriptor**	**Reported on Page #**
TITLE & ABSTRACT	1	How participants were allocated to interventions (*e.g.*, "random allocation", "randomised", or "randomly assigned").	Patients with coronary endothelial dysfunction, indicated by abnormal acetylcholine induced vasoconstriction, were randomly assigned to an exercise-training group or a control group.
INTRODUCTION Background	2	Scientific background and explanation of rationale.	Studies of the cardioprotective effects of exercise training in patients with coronary artery disease have yielded contradictory results. Exercise training has been associated with improvement in myocardial perfusion even in patients who have progression of coronary atherosclerosis. We therefore conducted a prospective study of the effect of exercise training on endothelial function in patients with coronary artery disease.
METHODS Participants	3	Eligibility criteria for participants and the settings and locations where the data were collected.	Patients were eligible for the stenosis that required nonsurgical revascularization (percutaneous transluminal coronary angioplasty) and a noncritical stenosis in another coronary vessel, which thus could be used for testing (the target vessel). To be suitable for testing, the target vessel had to have signs of endothelial dysfunction, defined as either constriction or no change in response to acetylcholine. Patients also had to have a symptom-free exercise capacity of at least 50 W. The protocol of this study was approved by the ethics committee of the University of Leipzig, and written informed consent was obtained from all patients before randomization.
Interventions	4	Precise details of the interventions intended for each group and how and when they were actually administered.	Patients assigned to exercise training stayed in the hospital for the initial four weeks of the study period. They were expected to exercise, under close supervision, six times per day for 10 minutes (in addition to 5 minutes for warming up and 5 minutes for cooling down during each session); they exercised on a bicycle ergometer at 80% percent of the heart rate they had reached during peak oxygen uptake in the initial

			exercise test. Patients assigned to the control group resumed treatment with their previous medications after the initial study, continued their sedentary lifestyle, and were supervised by their private physician.
Objectives	5	Specific objectives and hypotheses.	The objective of this study was to determine whether aerobic exercise training has the potential to correct endothelial dysfunction and improve coronary flow reserve in patients with coronary artery disease.
Outcomes	6	Clearly defined primary and secondary outcome measures and, when applicable, any methods used to enhance the quality of measurements (*e.g.*, multiple observations, training of assessors).	In patients with symptomatic coronary artery disease, endurance exercise training has been shown to attenuate ST-segment depression during exercise and decrease perfusion defects on thallium scanning, indicating a possible increase in myocardial perfusion. Advocates of exercise training for patients with coronary atherosclerosis have long faced the question of how exercise induces improvement in myocardial perfusion in the absence of any net regression of epicardial coronary stenosis. Recruitment of collateral vessels during maximal exercise is one possible mechanism, but angiographic studies performed in patients at rest have failed to provide support for this hypothesis.
Sample size	7	How sample size was determined and, when applicable, explanation of any interim analyses and stopping rules.	To minimize the effect of variables that could influence endothelial function, patients with any of the following conditions were excluded: diabetes, hypertension, hypercholesterolemia, cigarette smoking during the previous three months, ventricular tachyarrhythmia, chronic obstructive pulmonary disease, valvular heart disease, and a left ventricular ejection fraction of less than 40 percent. Patients who had undergone coronary-artery bypass graft surgery, had undergone a mechanical revascularization procedure during the previous three months, or had had myocardial infarction during the seven days before randomization were also excluded, as were patients with hematologic, renal, or hepatic dysfunction.
Randomization -- Sequence	8	Method used to generate the random allocation sequence, including details of any restrictions (*e.g.*,	Random assignment with no more details was used to allocate participants to either training or no training group.

generation		blocking, stratification)	
Randomization -- Allocation concealment	9	Method used to implement the random allocation sequence (*e.g*., numbered containers or central telephone), clarifying whether the sequence was concealed until interventions were assigned.	---
Randomization -- Implementation	10	Who generated the allocation sequence, who enrolled participants, and who assigned participants to their groups.	Allocation, sequence and enrolment were performed by the authors involved in the present investigation.
Blinding (masking)	11	Whether or not participants, those administering the interventions, and those assessing the outcomes were blinded to group assignment. If done, how the success of blinding was evaluated.	No information regarding blinding was mentioned
Statistical methods	12	Statistical methods used to compare groups for primary outcome(s); Methods for additional analyses, such as subgroup analyses and adjusted analyses.	All data are expressed as means ±SE. Both the absolute values and the percentage changes from base-line values were used in the statistical analyses; the two types of analysis yielded similar P values. Comparisons within each group and between the groups were performed with the use of two-way repeated-measures analysis of variance, followed by a post hoc Tukey test. Data were tested for normal distribution with the Kolmogorov–Smirnov test and for homogeneity of variances with Levene's test. The Mann–Whitney U test was used to compare the percentage changes (from the initial study to the follow-up assessment at four weeks) between the two treatment groups. A P value of less than 0.05 (by two-tailed testing) was considered to indicate statistical significance.
RESULTS Participant flow	13	Flow of participants through each stage (a diagram is strongly recommended). Specifically, for each group report the numbers of participants randomly assigned, receiving intended treatment, completing the study protocol, and analyzed for the primary outcome. Describe protocol deviations from study as planned, together with reasons.	A flow chart was not available
Recruitment	14	Dates defining the periods of recruitment and follow-up.	This article does not show the enrolment periods
Baseline data	15	Baseline demographic and clinical characteristics of	All demographic data and baseline characteristics were

		each group.	reported in table 1.
Numbers analyzed	16	Number of participants (denominator) in each group included in each analysis and whether the analysis was by "intention-to-treat". State the results in absolute numbers when feasible (*e.g.*, 10/20, not 50%).	10 patients were randomised to the intervention group and 9 patients to the control group.
Outcomes and estimation	17	For each primary and secondary outcome, a summary of results for each group, and the estimated effect size and its precision (*e.g.*, 95% confidence interval).	The two groups had similar vasoconstrictive responses to acetylcholine. After four weeks of exercise training, coronary-artery constriction in response to acetylcholine at a dose of 7.2 µg per minute was reduced by 54% with the change in the control group). In the exercise- training group, the increases in mean peak flow velocity in response to 0.072, 0.72, and 7.2 µg of acetylcholine. After four weeks of exercise, the increases in response to acetylcholine were 27±7, 73±19, and 142±28 percent.
Ancillary analyses	18	Address multiplicity by reporting any other analyses performed, including subgroup analyses and adjusted analyses, indicating those pre-specified and those exploratory.	---
Adverse events	19	All important adverse events or side effects in each intervention group.	No adverse event or side effect was mentioned.
DISCUSSION Interpretation	20	Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision and the dangers associated with multiplicity of analyses and outcomes.	Coronary atherosclerosis is associated with progressive impairment of coronary endothelial function. Since endothelium-derived nitric oxide is thought to be necessary to maintain an adequate vascular response to increased blood-flow demands during exercise, correction of endothelial dysfunction has become a goal of therapy.
Generalizability	21	Generalizability (external validity) of the trial findings.	Exercise training improves endothelium- dependent vasodilatation both in epicardial coronary vessels and in resistance vessels in patients with coronary artery disease
Overall evidence	22	General interpretation of the results in the context of current evidence.	Four weeks of vigorous exercise training improved coronary endothelial function in patients with asymptomatic coronary atherosclerosis. Coronary vasoconstriction in response to acetylcholine was significantly attenuated after exercise training, indicating that exercise had beneficial effects on the endothelium of epicardial conduit vessels. In agreement with

			this result was the finding that adenosine induced flow-dependent vasodilatation after training was markedly improved. These findings indicate that in the absence of clinically significant coronary artery stenosis, the vasodilatory capacity of coronary resistance vessels was enhanced.

Izawa et al. (2006)

PAPER SECTION **And topic**	**Item**	**Descriptor**	**Reported on Page #**
TITLE & ABSTRACT	1	How participants were allocated to interventions (*e.g.*, "random allocation", "randomised", or "randomly assigned").	Patients were randomly assigned to a muscle strength training or a control group
INTRODUCTION Background	2	Scientific background and explanation of rationale.	Cardiac rehabilitation is important to improve health-related quality of life and physiological measures such as peak oxygen uptake. In addition, supervised muscle strength training is also effective for both apparently healthy people and cardiac patients.
METHODS Participants	3	Eligibility criteria for participants and the settings and locations where the data were collected.	Subjects were selected from among 53 patients admitted to St. Marianna University School of Medicine Hospital for evaluation of MI. 48 met the criteria and were included in the study.
Interventions	4	Precise details of the interventions intended for each group and how and when they were actually administered.	Patients in the MS group performed an unsupervised exercise program at least twice weekly for 1 jour that combined walking as aerobic exercise and resistance training. Exercise sessions were composed of warm-up, aerobic exercise, resistance training and cool-down periods. Exercise intensity during aerobic exercise was maintained at a rating of perceived exertion of 11 to 13 according to the Borg 6 to 20 scale. The control group also met at least twice weekly for 1 hour in an unsupervised aerobic exercise program comprised of walking but no MS training. Exercise sessions were composed of warm-up, aerobic exercise and cool-down periods. Exercise intensity during aerobic exercise was maintained at a rating of perceived exertion of 11 to 13 during walking. Each session was also preceded and followed by series of upper and lower extremity and body stretches.
Objectives	5	Specific objectives and hypotheses.	The purpose of the present study was to evaluate the effect of unsupervised exercise training on exercise maintenance and physical activity and the effect of muscle strength training

			on physiological measures over the 6-month period following supervised cardiac rehabilitation.
Outcomes	6	Clearly defined primary and secondary outcome measures and, when applicable, any methods used to enhance the quality of measurements (*e.g.*, multiple observations, training of assessors).	Although many reports relate the effectiveness of supervised cardiac rehabilitation, long-term maintenance of compliance after supervised cardiac rehabilitation ends has proven to be a problem. Cardiac rehabilitation in Japan is covered by national health insurance for the first 6 months after acute MI and thereafter, patients must continue further exercise at their own volition.
Sample size	7	How sample size was determined and, when applicable, explanation of any interim analyses and stopping rules.	Of 53 patients, 48 met the criteria and were included in the study. The other 5 patients were excluded due to inability to complete exercise testing because of cerebrovascular disease, orthopaedic disorder or heart failure during an initial 3-week post MI cardiac rehabilitation program. From these 48 patients, 37 were recruited following completion of a 5-month outpatient recovery-phase cardiac rehabilitation and exercise testing. 24 of these 37 patients were offered participation and the remaining 13 had no interest, did not have enough time, or had changed hospitals.
Randomization -- Sequence generation	8	Method used to generate the random allocation sequence, including details of any restrictions (*e.g.*, blocking, stratification)	Random assignment with no more details was used to allocate participants to either training or no training group.
Randomization -- Allocation concealment	9	Method used to implement the random allocation sequence (*e.g.*, numbered containers or central telephone), clarifying whether the sequence was concealed until interventions were assigned.	---
Randomization -- Implementation	10	Who generated the allocation sequence, who enrolled participants, and who assigned participants to their groups.	Allocation, sequence and enrolment were performed by the authors involved in the present investigation.
Blinding (masking)	11	Whether or not participants, those administering the interventions, and those assessing the outcomes were blinded to group assignment. If done, how the success of blinding was evaluated.	No information regarding blinding was mentioned.
Statistical methods	12	Statistical methods used to compare groups for primary outcome(s); Methods for additional analyses, such as	Results are expressed as mean ±1 standard deviation. Non-parametric and χ^2 tests were used to analyze differences in

		subgroup analyses and adjusted analyses.	clinical factors between groups. Physical activity and physiological outcomes were analysed using repeated-measures analysis of variance (ANOVA). ANOVA was used to compare main or interaction effects over time for period and group. For each ANOVA model with a significant main or interaction effect, Tukey HSD tests were performed post hoc to localize the effects. Statistical analyses were performed with SPSS 12.0J statistical software. A p value of <0.05 was considered significant.
RESULTS Participant flow	13	Flow of participants through each stage (a diagram is strongly recommended). Specifically, for each group report the numbers of participants randomly assigned, receiving intended treatment, completing the study protocol, and analyzed for the primary outcome. Describe protocol deviations from study as planned, together with reasons.	A flow chart was not available
Recruitment	14	Dates defining the periods of recruitment and follow-up.	Between April 2002 and October 2002.
Baseline data	15	Baseline demographic and clinical characteristics of each group.	All demographic data and baseline characteristics were reported in table 1.
Numbers analyzed	16	Number of participants (denominator) in each group included in each analysis and whether the analysis was by "intention-to-treat". State the results in absolute numbers when feasible (*e.g.*, 10/20, not 50%).	All 10 (100%) of the MS group patients and all 8 (100%) of the control patients continued exercise over the 6-month period of unsupervised exercise training.
Outcomes and estimation	17	For each primary and secondary outcome, a summary of results for each group, and the estimated effect size and its precision (*e.g.*, 95% confidence interval).	Baseline measurements of physical activity, peak oxygen consumption and muscle strength were performed at the end of supervised recovery phase cardiac rehabilitation (6 months after the onset of myocardial infarction: T1). 6 months later, after going through an unsupervised exercise program (12 months after the onset of myocardial infarction: T2) exercise maintenance, peak oxygen consumption, muscle strength and physical activity were re-measured. There were no significant differences in physical activity between the MS group and the control group.
Ancillary analyses	18	Address multiplicity by reporting any other analyses performed, including subgroup analyses and adjusted	---

		analyses, indicating those pre-specified and those exploratory.	
Adverse events	19	All important adverse events or side effects in each intervention group.	No adverse events or side effects were mentioned. The study was limited by the small number of patients, no investigation of the patients who had not participated in this study at T2 and unavoidable differences in environment between the two groups.
DISCUSSION Interpretation	20	Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision and the dangers associated with multiplicity of analyses and outcomes.	Self recording of physical activity during exercise maintenance in the unsupervised exercise training period may have contributed to the continuance of exercise in our patients.
Generalizability	21	Generalizability (external validity) of the trial findings.	The performance of aerobic walking exercise in addition to MS training during an unsupervised period following supervised cardiac rehabilitation may effectively maintain exercise capacity and increase muscle strength.
Overall evidence	22	General interpretation of the results in the context of current evidence.	The study was one of the first randomised controlled trials to investigate the effect of a combined mode of unsupervised exercise training (walking and muscle strengthening using body weight) on physical activity and physiological measures after supervised cardiac rehabilitation. The exercise training program was continued by all patients after completion of formal, supervised cardiac rehabilitation.

Lee et al. (2008)

PAPER SECTION **And topic**	**Item**	**Descriptor**	**Reported on Page #**
TITLE & ABSTRACT	1	How participants were allocated to interventions (*e.g.*, "random allocation", "randomised", or "randomly assigned").	Post-infarction patients were randomly assigned to a training group or a non training group.
INTRODUCTION Background	2	Scientific background and explanation of rationale.	Cardiac rehabilitation is believed to increase myocardial perfusion reserve (MPR) but this has not been adequately studied because of poor delineation of infarcted myocardium in previous studies. The purpose of this study was to determine the effect of cardiac rehabilitation on myocardial perfusion reserve with contrast-enhanced magnetic resonance imaging.
METHODS Participants	3	Eligibility criteria for participants and the settings and locations where the data were collected.	Men aged ≤65 years old with a history of myocardial infarction for at least 3months before screening were eligible. The inclusion criteria were a successful procedural outcome after primary stenting during the initial myocardial infarction treatment, a clinically stable course for at least 3 months after discharge and no evidence of myocardial ischemia on initial and follow-up exercise testing. This study was performed at the National Taiwan University Hospital.
Interventions	4	Precise details of the interventions intended for each group and how and when they were actually administered.	At the baseline and 3-month follow-up assessment, all patients underwent a functional evaluation, which included clinical evaluation, exercise testing and cardiac magnetic resonance imaging.
Objectives	5	Specific objectives and hypotheses.	The primary aim of the present study was to investigate whether cardiac rehabilitation influences perfusion differently in the infarcted and remote myocardium. The secondary aim was to assess the relation between myocardial perfusion reserve and exercise capacity.
Outcomes	6	Clearly defined primary and secondary outcome measures	Cardiac magnetic resonance imaging is an excellent diagnostic tool for serial assessment of changes in left ventricular structure and function, infarct location and size, and myocardial perfusion reserve. The ability of cardiac

			magnetic resonance imaging to assess concurrently and with high spatial resolution the extent of scar tissue in the myocardium and perfusion is one of the major strengths of this technique.
Sample size	7	How sample size was determined and, when applicable, explanation of any interim analyses and stopping rules.	39 patients were enrolled. After completing the initial evaluation, they were randomly assigned to the 3-month training program (n=20) or the non-training group (n=19). For comparison of exercise capacity and myocardial perfusion, 19 age-, weight-, and height- matched subjects without cardiovascular risk factors were selected as healthy controls.
Randomization -- Sequence generation	8	Method used to generate the random allocation sequence, including details of any restrictions (*e.g.*, blocking, stratification)	Random assignment with no more details was used to allocate participants to either training or no training group.
Randomization -- Allocation concealment	9	Method used to implement the random allocation sequence (*e.g.*, numbered containers or central telephone), clarifying whether the sequence was concealed until interventions were assigned.	---
Randomization -- Implementation	10	Who generated the allocation sequence, who enrolled participants, and who assigned participants to their groups.	Allocation, sequence and enrolment were performed by the authors involved in the present investigation.
Blinding (masking)	11	Whether or not participants, those administering the interventions, and those assessing the outcomes were blinded to group assignment. If done, how the success of blinding was evaluated.	No information regarding blinding was mentioned
Statistical methods	12	Statistical methods used to compare groups for primary outcome(s); Methods for additional analyses, such as subgroup analyses and adjusted analyses.	Calculations of statistical power for the primary end point of the peak VO_2 based on previous data in post- myocardial infarction patients showed that a power of 0.8 was needed to detect a 14% increase at a 5% significance level with a minimum of 17 subjects per group. All data are presented as the mean± standard deviation for continuous data and as proportions of binary data. If the data were not distributed normally, natural logarithmic transformation was used for analysis. Correlations were tested using Pearson analysis. Baseline characteristics were compared using the unpaired Student's *t* test for continuous data and chi-square analysis

			for binary data. Changes in data from the baseline to follow-up assessments were compared using the paired Student's *t* test. A p <0.05 was considered statistically significant.
RESULTS Participant flow	13	Flow of participants through each stage (a diagram is strongly recommended). Specifically, for each group report the numbers of participants randomly assigned, receiving intended treatment, completing the study protocol, and analyzed for the primary outcome. Describe protocol deviations from study as planned, together with reasons.	A flow chart was not available
Recruitment	14	Dates defining the periods of recruitment and follow-up.	This article does not show the enrolment periods but does indicate that this study was performed between August 2004 and December 2005.
Baseline data	15	Baseline demographic and clinical characteristics of each group.	All demographic data and baseline characteristics for the 39 post myocardial patients were reported in table 1.
Numbers analyzed	16	Number of participants (denominator) in each group included in each analysis and whether the analysis was by "intention-to-treat". State the results in absolute numbers when feasible (*e.g.*, 10/20, not 50%).	Of 91 patients who were screened for possible enrolment, 37 refused to participate and 15 did not meet the inclusion criteria because of exertional angina (n=3), sustained ventricular arrhythmias (n=3) or exercise-limiting diseases (n=9). The remaining 39 patients were enrolled and were randomly assigned to the 3-month training program (n=20) or to the nontraining group (n=19).
Outcomes and estimation	17	For each primary and secondary outcome, a summary of results for each group, and the estimated effect size and its precision (*e.g.*, 95% confidence interval).	In the training group, exercise capacity increased by 15% ($p<0.01$), to the same level as in healthy controls. The post-training myocardial perfusion reserve increased in both remote (30%, $p<0.01$) and infarcted myocardium (25%, $p<0.05$) and reached the same level as in healthy controls. The change in exercise capacity correlated with the change in myocardial perfusion reserve in the remote myocardium ($r=0.55$, $p<0.001$ for peak VO_2). In the nontraining group, exercise capacity and myocardial perfusion reserve were unchanged.
Ancillary analyses	18	Address multiplicity by reporting any other analyses performed, including subgroup analyses and adjusted analyses, indicating those pre-specified and those	---

		exploratory.	
Adverse events	19	All important adverse events or side effects in each intervention group.	No patient died, was hospitalized for coronary intervention or had worsening symptoms.
DISCUSSION Interpretation	20	Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision and the dangers associated with multiplicity of analyses and outcomes.	Cardiac rehabilitation improves perfusion reserve in both infarcted and remote myocardium, with a parallel increase in exercise capacity.
Generalizability	21	Generalizability (external validity) of the trial findings.	In routine clinical practice, cardiac rehabilitation will begin as soon as possible after a cardiac event. However, studying patients soon after acute myocardial infarction is complicated and given this study purpose and design only patients with stable myocardial infarction were chosen. Moreover, only men were enrolled so further studies should be performed on women. Last but not least, patients were treated for 3 months only and the long-term effects of cardiac rehabilitation on these parameters remain unknown.
Overall evidence	22	General interpretation of the results in the context of current evidence.	Three months of cardiac rehabilitation at a moderate intensity resulted in an improvement in exercise capacity to the same level as in healthy controls and rehabilitation also increased myocardial perfusion reserve in both the remote and infarcted myocardium to the same level as in healthy subjects. The change in exercise capacity correlated positively with that the myocardial perfusion reserve in the remote myocardium and left ventricular dimension, function, wall stress or infarct size did not change during the study period.

Leizorovicz et al. (1991)

PAPER SECTION **And topic**	**Item**	**Descriptor**	**Reported on Page #**
TITLE & ABSTRACT	1	How participants were allocated to interventions (*e.g.*, "random allocation", "randomised", or "randomly assigned").	Male post myocardial infarction patients under 65 years old were randomised 30 to 60 days after the acute event into a 6-week rehabilitation programme (RP), a counselling programme without exercise training (CP) and usual care (UC).
INTRODUCTION Background	2	Scientific background and explanation of rationale.	About 20 years ago exercise rehabilitation was proposed for the management of patients who had had a myocardial infarction. Although its safety, benefit, and exercise tolerance seem now established, its efficacy for long-term survival, morbidity and quality of life remains controversial. Several randomised, controlled trials of rehabilitation programmes after myocardial infarction have been published but due to their limited statistical power none gave definite answers. However, meta analyses of all randomised trials have indicated a modest but favourable trend in mortality.
METHODS Participants	3	Eligibility criteria for participants and the settings and locations where the data were collected.	Only male patients under 65 years with a typical myocardial infarction, no major irreversible complication or disability, were retained for further evaluation, provided they agreed to the principle of the study. Patients were not randomised if they had contraindication to exercise testing i.e., recent stroke, disability of lower limbs, uncontrolled heart failure, severe rhythm disturbances, high blood pressure >180mmHg, severe angina pectoris, or abnormalities triggered by the baseline exercise test
Interventions	4	Precise details of the interventions intended for each group and how and when they were actually administered.	The rehabilitation programme started within a few days of randomization. It spanned 6 weeks and included: three training sessions a week on a cycloergometer; walking; gymnastic and respiratory physiotherapy; relaxation; recommendations on control of cardiovascular risk factors (smoking habits, diet); recommendations to continue regular physical training at the end of the 6-week programme.

			Each training session consisted of a 25-min exercise test on a cycloergometer. The workload was set to reach 80% of the maximal heart rate as evaluated by the baseline test. Workload was then decreased progressively over 2 min; stopping criteria were the same as those for an exercise test (ST depression ^2 mm and/or VPB >10/min and/or pain). Maximal workload was increased as the sessions progressed.
Objectives	5	Specific objectives and hypotheses.	The objective is to present the findings of the patients who could benefit from the active rehabilitation programme
Outcomes	6	Clearly defined primary and secondary outcome measures and, when applicable, any methods used to enhance the quality of measurements (*e.g.*, multiple observations, training of assessors).	An important component of the rehabilitation programme seems nevertheless to have been overlooked since most of these programmes included counselling on diet, smoking and psychological support, as well as close medical follow-up. A randomised trial was set up to compare long-term functional capacity and quality of life for post myocardial infarction patients as a result of three care programmes: rehabilitation, counselling and usual care; secondary end points were mortality and non-fatal cardiac events
Sample size	7	How sample size was determined and, when applicable, explanation of any interim analyses and stopping rules.	1308 patients were admitted to the participating coronary care units with a suspected myocardial infarction.
Randomization -- Sequence generation	8	Method used to generate the random allocation sequence, including details of any restrictions (*e.g.*, blocking, stratification)	Random assignment with no more details was used to allocate participants to either training or no training group
Randomization -- Allocation concealment	9	Method used to implement the random allocation sequence (*e.g.*, numbered containers or central telephone), clarifying whether the sequence was concealed until interventions were assigned.	---
Randomization -- Implementation	10	Who generated the allocation sequence, who enrolled participants, and who assigned participants to their groups.	Allocation, sequence and enrolment were performed by the authors involved in the present investigation
Blinding (masking)	11	Whether or not participants, those administering the interventions, and those assessing the outcomes were blinded to group assignment. If done, how the success	No information regarding blinding was mentioned

		of blinding was evaluated.	
Statistical methods	12	Statistical methods used to compare groups for primary outcome(s); Methods for additional analyses, such as subgroup analyses and adjusted analyses.	Comparisons of the three groups were performed using the classical statistical tests, χ^2, exact Fisher test, and one-way analysis of variance. The analysis followed the intention-to-treat principle; patients were counted in the group to which they were allocated
RESULTS Participant flow	13	Flow of participants through each stage (a diagram is strongly recommended). Specifically, for each group report the numbers of participants randomly assigned, receiving intended treatment, completing the study protocol, and analyzed for the primary outcome. Describe protocol deviations from study as planned, together with reasons.	No flow chart was available
Recruitment	14	Dates defining the periods of recruitment and follow-up.	This article does not show the enrolment periods but does indicate that this study was performed From February 1981 to May 1984
Baseline data	15	Baseline demographic and clinical characteristics of each group.	All demographic data and baseline characteristics for the post myocardial patients were reported in table 1.
Numbers analyzed	16	Number of participants (denominator) in each group included in each analysis and whether the analysis was by "intention-to-treat". State the results in absolute numbers when feasible (*e.g.*, 10/20, not 50%).	182 were eventually randomised to the three groups UC (n = 61), CP (n = 61), RP (n = 60).
Outcomes and estimation	17	For each primary and secondary outcome, a summary of results for each group, and the estimated effect size and its precision (*e.g.*, 95% confidence interval).	The percentage of patients reaching the maximal heart rate at exercise test was higher in the RP group even after 2 years. The number of deaths at 2 years was respectively 4, 5 and 0 in the UC, CP and RP groups.
Ancillary analyses	18	Address multiplicity by reporting any other analyses performed, including subgroup analyses and adjusted analyses, indicating those pre-specified and those exploratory.	---
Adverse events	19	All important adverse events or side effects in each intervention group.	Exclusion of women and men above the age of 65 alone contributed to almost 60% of all reasons of non eligibility. Early deaths, early complications of myocardial infarction, refusal or impossibility of participating account for a further 20% of exclusions.

DISCUSSION Interpretation	20	Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision and the dangers associated with multiplicity of analyses and outcomes.	A structured counselling programme, although less expensive and more widely practicable, failed to show any benefit
Generalizability	21	Generalizability (external validity) of the trial findings.	Knowledge of which myocardial infarction patients are eligible for a rehabilitation programme might help when discussing the socio-economical impact of such programmes. Admittedly they might concern only a small proportion of all myocardial infarction patients with a good vital prognosis. On the other hand, a rehabilitation programme is limited in time, 6 weeks, and its cost might be considered moderate especially in view of the possible maintenance of benefits over several years.
Overall evidence	22	General interpretation of the results in the context of current evidence.	The P.RE.COR study confirmed the short as well as the long-term benefit of a rehabilitation programme on exercise tolerance and survival in patients having had a myocardial infarction. No effect could be seen on return to work or long-term modification of life style. In view of the previously reported randomised trials and of the present study, the tested rehabilitation programme seems worth recommending in myocardial infarction patients with uncomplicated myocardial infarction.

Marchionni et al. (2003)

PAPER SECTION **And topic**	**Item**	**Descriptor**	**Reported on Page #**
TITLE & ABSTRACT	1	How participants were allocated to interventions (*e.g.*, "random allocation", "randomised", or "randomly assigned").	Patients were randomised to a hospital-cr group, a home-cr group and a control group.
INTRODUCTION Background	2	Scientific background and explanation of rationale.	Whether cardiac rehabilitation (CR) is effective in patients older than 75 years, who have been excluded from most trials, remains unclear.
METHODS Participants	3	Eligibility criteria for participants and the settings and locations where the data were collected.	Patients older than 45 years consecutively referred to our CR unit by 4 of the 6 intensive care units in the Florence area for functional evaluation 4 to 6 weeks after MI over a 48-month period were eligible if they had none of the following exclusion criteria: severe cognitive impairment or physical disability, left ventricular ejection fraction <35%, contraindications to vigorous physical exercise, eligibility for myocardial revascularization because of low-effort myocardial ischemia, refusal, or living too far from the CR unit. An ad hoc ethics committee approved the trial, informed consent was systematically obtained, and a letter describing the trial design was delivered to patients' family physicians.
Interventions	4	Precise details of the interventions intended for each group and how and when they were actually administered.	The Hosp-CR program consisted of 40 exercise sessions: 24 sessions (3/wk) of endurance training on a cycle ergometer (5-minute warm-up, 20-minute training at constant workload, 5-minute cool down, and 5-minute post-exercise monitoring) plus 16 (2/wk) 1-hour sessions of stretching and flexibility exercises. In both sessions, ECG was monitored by telemetry, and exercise intensity was set at 70% to 85% of heart rate attained during baseline symptom-limited exercise test. Patients received cardiovascular risk factor management counselling twice per week and were invited to join a monthly support group together with family members. Patients randomised to Home-CR participated in 4 to 8 supervised instruction sessions in the CR unit, where they were taught

			necessary precautions and how to perform their training at home. Patients received cardiovascular risk factor management counselling at each in-hospital session and were invited to join a monthly family oriented support group.
Objectives	5	Specific objectives and hypotheses.	2 months of post-MI Hosp-CR or Home-CR would improve exercise tolerance (primary outcome) compared with no CR (control) and that the extent of this improvement would be independent of age. Secondary objectives of the trial included a comparison of the effects of Hosp-CR and Home-CR on HRQL and on healthcare utilization.
Outcomes	6	Clearly defined primary and secondary outcome measures and, when applicable, any methods used to enhance the quality of measurements (*e.g.*, multiple observations, training of assessors).	Only limited age-specific data are available from trials with an average patient age <75 years and from observational studies of post-MI CR with small numbers of patients <75 years of age. In particular, whether CR improves exercise tolerance similarly in patients younger and older than 75 years remains uncertain. Indeed, with only 6% of 778 patients <75 years of age in the largest observational study, its conclusion of a similar percent improvement in exercise tolerance after training in patients younger and older than 75 years is questionable. Furthermore, whether CR has positive effects on HRQL has received limited attention in older post-MI patients. Mobility problems and difficulties in using public transportation may limit the participation in outpatient, supervised, hospital-based CR (Hosp-CR) of older individuals for whom home-based CR (Home-CR) might be a valid alternative. In selected low-risk, middle-aged post-MI patients, Home-CR is safe and effective, 18 but its feasibility and efficacy have never been explored in older adults.
Sample size	7	How sample size was determined and, when applicable, explanation of any interim analyses and stopping rules.	Of 773 screened for eligibility, 270 patients were enrolled, and 503 were excluded for cardiological reasons, comorbidities that contraindicated vigorous physical exercise, disability or cognitive impairment and refusal or logistic reasons. More very old patients were excluded for comorbidities or disability/cognitive impairment with similar exclusion rates for cardiological reasons and for

			refusal or logistic reasons
Randomization -- Sequence generation	8	Method used to generate the random allocation sequence, including details of any restrictions (*e.g.*, blocking, stratification)	Random assignment with no more details was used to allocate participants to either training or no training group.
Randomization -- Allocation concealment	9	Method used to implement the random allocation sequence (*e.g.*, numbered containers or central telephone), clarifying whether the sequence was concealed until interventions were assigned.	---
Randomization -- Implementation	10	Who generated the allocation sequence, who enrolled participants, and who assigned participants to their groups.	Allocation, sequence and enrolment were performed by the authors involved in the present investigation.
Blinding (masking)	11	Whether or not participants, those administering the interventions, and those assessing the outcomes were blinded to group assignment. If done, how the success of blinding was evaluated.	Testing personnel were blinded to patients assignments
Statistical methods	12	Statistical methods used to compare groups for primary outcome(s); Methods for additional analyses, such as subgroup analyses and adjusted analyses.	Data were analyzed with SPSS version 10.1 for Windows, with a 2-sided *P* value <0.05 considered statistically significant. The associations between age and categorical or continuous variables were tested by ANOVA. Changes in TWC and SIP score were compared across treatment and age groups with general linear models for repeated measures. Age-treatment interactions were tested by calculating regression models for each outcome variable, with dummy variables for age and treatment groups and interaction terms.
RESULTS Participant flow	13	Flow of participants through each stage (a diagram is strongly recommended). Specifically, for each group report the numbers of participants randomly assigned, receiving intended treatment, completing the study protocol, and analyzed for the primary outcome. Describe protocol deviations from study as planned, together with reasons.	A flow chart was available.
Recruitment	14	Dates defining the periods of recruitment and follow-up.	No enrolment periods were mentioned.
Baseline data	15	Baseline demographic and clinical characteristics of each group.	All data were presented in table 1.

Numbers analyzed	16	Number of participants (denominator) in each group included in each analysis and whether the analysis was by "intention-to-treat". State the results in absolute numbers when feasible (*e.g.*, 10/20, not 50%).	In total, 38 patients dropped out: 10 died (1 sudden death, 2 reinfarction, 3 neoplasm, 1 pulmonary embolism, 1 peri-operatively after CABG, and 2 undetermined), 7 had nonfatal events (2 reinfarction, 2 CABG, 1 unstable angina, 1 congestive heart failure, and 1 new onset of cognitive problems), and 21 refused to continue the study (14 of 21 within the first 2 months).
Outcomes and estimation	17	For each primary and secondary outcome, a summary of results for each group, and the estimated effect size and its precision (*e.g.*, 95% confidence interval).	Within each age group, TWC improved with Hosp-CR and Home-CR and was unchanged with no CR. The improvement was similar in middle-aged and old persons but smaller, although still significant, in very old patients. TWC reverted toward baseline by 12 months with Hosp-CR but not with Home-CR. HRQL improved in middle-aged and old CR and control patients but only with CR in very old patients
Ancillary analyses	18	Address multiplicity by reporting any other analyses performed, including subgroup analyses and adjusted analyses, indicating those pre-specified and those exploratory.	---
Adverse events	19	All important adverse events or side effects in each intervention group.	No adverse events or side effects were mentioned.
DISCUSSION Interpretation	20	Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision and the dangers associated with multiplicity of analyses and outcomes.	Post-MI Hosp-CR and Home-CR are similarly effective in the short term and improve TWC and HRQL in each age group. However, with lower costs and more prolonged positive effects, Home-CR may be the treatment of choice in low-risk older patients.
Generalizability	21	Generalizability (external validity) of the trial findings.	Despite these limitations, the CR-AGE trial provides original information on the efficacy of post-MI CR in older patients. First, we demonstrated that the physiological response to CR is attenuated in patients older than 75 years. Additional research will demonstrate whether very old patients need a longer duration of CR for optimal physiological benefit. Second, the need for designing CR interventions with less rigid admission criteria and a lower intensity exercise prescription is reinforced by the age-related increase in the exclusion rate from the present trial. Finally,

			the present findings suggest that post-MI Home-CR is cost-effective and may be preferable in very old, low-risk patients. Assignment of lower-risk individuals to Home-CR programs would imply that larger numbers of medium- and high-risk, frail older patients would have access to the limited available resources presently concentrated on Hosp-CR.
Overall evidence	22	General interpretation of the results in the context of current evidence.	The results of this trial confirmed our first study hypothesis that compared with no CR, post-MI CR enhances exercise tolerance in patients of all ages, including those older than 75 years and as old as 86 years, who have been excluded from most previous trials. Their second study hypothesis was not confirmed.

Maroto Montero et al. (2005)

PAPER SECTION **And topic**	**Item**	**Descriptor**	**Reported on Page #**
TITLE & ABSTRACT	1	How participants were allocated to interventions (*e.g.*, "random allocation", "randomised", or "randomly assigned").	Patients were randomly assigned into a comprehensive cardiac rehabilitation program or a control group.
INTRODUCTION Background	2	Scientific background and explanation of rationale.	The application of cardiac rehabilitation programs (CRP) following acute myocardial infarction (AMI) has demonstrated their efficacy in increasing functional capacity, controlling coronary risk factors, reducing symptoms and countering psychological deterioration. They have also been shown to improve cost-efficiency.
METHODS Participants	3	Eligibility criteria for participants and the settings and locations where the data were collected.	180 consecutive male patients diagnosed with AMI and admitted to the coronary care unit of our hospital. Enrolments were based on the American Association of Cardiovascular and Pulmonary Rehabilitation inclusion criteria: age <65 years, low risk (hospital course without complications, absence of signs of myocardial ischemia, functional capacity >7 metabolic equivalent time [MET], ejection fraction >50% and absence of severe ventricular arrhythmias). All patients gave signed informed consent according to unit procedure and the study was approved by our hospital ethics committee
Interventions	4	Precise details of the interventions intended for each group and how and when they were actually administered.	Physical training consisted of 3 1 hour sessions per week in the hospital gym. At each session, patients followed a table of physiotherapy and aerobic training on mats or an exercise bicycle. During training, heart rate was calculated individually following stress exercise treadmill tests (Bruce protocol) at the start and end of the program. The initial test served to filter enrolments and patients with ischemia and low exercise levels were excluded and indicated for coronary angiography. Patients with exercise tests without signs of ischemia had their target heart rate set at 75% of the maximum achieved

			for the first 6 weeks of training and 85% for the last 6 weeks. Supervised training was complemented by progressively increasing daily walks of 1 hour in duration, when patients tried to maintain the heart rate achieved during training. Walks were undertaken by patients individually and were unsupervised.
Objectives	5	Specific objectives and hypotheses.	Their principal objective was to analyze and compare incidence of death in both groups at 10-year follow up; the secondary objective was to analyze complications occurring in the same period.
Outcomes	6	Clearly defined primary and secondary outcome measures and, when applicable, any methods used to enhance the quality of measurements (*e.g.*, multiple observations, training of assessors).	Given that ischemic heart disease is a progressive, chronic illness and that low-risk patients are included in CRP, possible beneficial effects of these therapeutic programs on morbidity and mortality require long-term evaluation. The present study was designed to compare the clinical evolution of 2 groups of patients with AMI: one following our multidisciplinary CRP and the other receiving conventional treatment.
Sample size	7	How sample size was determined and, when applicable, explanation of any interim analyses and stopping rules.	Patients were excluded on grounds of age and gender because of evidence that very few women are found with infarction and in an age range lower than that described. We set the age limit at 65 years, retirement age, because a high percentage of older patients abandon CRP for a variety of reasons.
Randomization -- Sequence generation	8	Method used to generate the random allocation sequence, including details of any restrictions (*e.g.*, blocking, stratification)	Random assignment with no more details was used to allocate participants to either training or no training group.
Randomization -- Allocation concealment	9	Method used to implement the random allocation sequence (*e.g.*, numbered containers or central telephone), clarifying whether the sequence was concealed until interventions were assigned.	---
Randomization -- Implementation	10	Who generated the allocation sequence, who enrolled participants, and who assigned participants to their groups.	Allocation, sequence and enrolment were performed by the authors involved in the present investigation.
Blinding (masking)	11	Whether or not participants, those administering the	No information regarding blinding was mentioned.

		interventions, and those assessing the outcomes were blinded to group assignment. If done, how the success of blinding was evaluated.	
Statistical methods	12	Statistical methods used to compare groups for primary outcome(s); Methods for additional analyses, such as subgroup analyses and adjusted analyses.	Chi-squared was used to compare percentages. In both groups, we calculated Kaplan-Meier survival curves and compared these using log-rank tests. Values of *P*<.05 were considered statistically significant.
RESULTS Participant flow	13	Flow of participants through each stage (a diagram is strongly recommended). Specifically, for each group report the numbers of participants randomly assigned, receiving intended treatment, completing the study protocol, and analyzed for the primary outcome. Describe protocol deviations from study as planned, together with reasons.	A flow chart was available
Recruitment	14	Dates defining the periods of recruitment and follow-up.	No enrolment periods were mentioned but the enrolment lasted 2 years
Baseline data	15	Baseline demographic and clinical characteristics of each group.	All data were presented in table 1.
Numbers analyzed	16	Number of participants (denominator) in each group included in each analysis and whether the analysis was by "intention-to-treat". State the results in absolute numbers when feasible (*e.g.*, 10/20, not 50%).	520 patients with AMI were admitted to the hospital coronary unit. We excluded those who did not fulfil the previously described criteria. After initial exercise tests, 10 patients were excluded with indication for coronary angiography due to signs of ischemia at low load levels. The remaining 180 were randomised into 2 groups of 90: 1 group (RG) followed the CRP and the other (CG) served as a reference. The 180 patients were randomised into 2 groups: one followed our cardiac rehabilitation program (RG) and the other, the control group (CG), received conventional treatment and served as a point of reference. At 10-year check-up, 11 patients had been lost (7 RG and 4 CG), leaving 83 and 86 patients, respectively
Outcomes and estimation	17	For each primary and secondary outcome, a summary of results for each group, and the estimated effect size and its precision (*e.g.*, 95% confidence interval).	All-cause mortality was significantly lower in the intervention group: the 10-year survival rate was 91.8% in the intervention group compared with 81.7% in the control group. There was

			also a decrease in cardiovascular mortality, though it was not statistically significant: the 10-year survival rate was 91.8% in the intervention group compared with 83.8% in the control group. The incidence of non-fatal complications was lower in the intervention group as was the incidence of unstable angina and cardiac heart failure and the need for coronary intervention.
Ancillary analyses	18	Address multiplicity by reporting any other analyses performed, including subgroup analyses and adjusted analyses, indicating those pre-specified and those exploratory.	---
Adverse events	19	All important adverse events or side effects in each intervention group.	No adverse event or side effects were mentioned.
DISCUSSION Interpretation	20	Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision and the dangers associated with multiplicity of analyses and outcomes.	The application of a comprehensive cardiac rehabilitation program significantly decreased long term mortality and morbidity in low-risk patients after acute myocardial infarction.
Generalizability	21	Generalizability (external validity) of the trial findings.	Modification of lifestyle behaviours such as smoking, eating abundant quantities of fats, sedentary habits, and methods of dealing with stress, can significantly reduce risk of coronary heart disease. Similarly, better fulfilment of therapeutic guidelines to treat hypertension, diabetes and dyslipidemia can prevent the appearance or progression of atherosclerosis. According to some estimates, >50% of the reduction in mortality due to coronary artery disease is attributable to behaviour changes.
Overall evidence	22	General interpretation of the results in the context of current evidence.	The results of our study support the hypothesis that a multifactor CRP with secondary prevention measures maintained in the long-term favourably influences prognosis in post-AMI patients. Their data are of interest because they show results in Spain where incidence of ischemic heart disease is clearly lower than in northern Europe.

Oldridge et al. (1990)

PAPER SECTION **And topic**	**Item**	**Descriptor**	**Reported on Page #**
TITLE & ABSTRACT	1	How participants were allocated to interventions (*e.g.*, "random allocation", "randomised", or "randomly assigned").	Patients were randomised to either an exercise conditioning and behavioral counseling or to conventional care.
INTRODUCTION Background	2	Scientific background and explanation of rationale.	Comprehensive cardiac rehabilitation may be considered as the sum of various efforts to modify cardiovascular risk factors and to assist patients in regaining their normal place in the community and in leading active and productive lives. Secondary prevention programs, designed to modify hypercholesterolemia, hypertension and cigarette smoking, also have been shown to reduce the likelihood of recurrent AMI.
METHODS Participants	3	Eligibility criteria for participants and the settings and locations where the data were collected.	All patients admitted with a diagnosis of AM1 to any 1 of 6 local hospitals were screened for eligibility. Criteria for a positive diagnosis of AM1 included typical chest discomfort, electrocardiographic changes compatible with AMI, and a significant rise in creatine phosphokinase (1.5 times normal upper limit or positive creatine phosphokinase & enzymes). Patients scoring <5 on the short form of the Beck Depression Inventory or <43 on the Spielberger State Anxiety Inventory or <42 on the Spielberger Trait Anxiety Inventory while still in hospital were not considered eligible for the trial; patients with evidence suggestive of major depression or anxiety were referred for further assessment. The study received approval from the ethics committees of the University and each hospital, and both patient and physician consent for participation in the trial were obtained.
Interventions	4	Precise details of the interventions intended for each group and how and when they were actually administered.	Participants attended 50- minute exercise sessions 2 times per week for 8 consecutive weeks. There was a 10-minute group warm-up at the beginning of each session; stationary cycle ergometer, treadmill walking and arm ergometer followed for 20 to 30 minutes. A cool-down, involving low-

			intensity activities, concluded the exercise session. The exercise prescription was based initially on 65% of the maximal heart rate response achieved during the exercise test. The rating of perceived exertion during exercise was a second criterion for effective training and safety.
Objectives	5	Specific objectives and hypotheses.	A randomised clinical trial of 8 weeks of comprehensive cardiac rehabilitation in patients who demonstrated moderate levels of depression or anxiety, beginning within 6 weeks after AMI was performed. Disease-specific and generic measures of health-related quality of life were used as the primary outcome measures to compare treatment with conventional care.
Outcomes	6	Clearly defined primary and secondary outcome measures and, when applicable, any methods used to enhance the quality of measurements (*e.g.*, multiple observations, training of assessors).	Only a few trials have addressed the issue with little or no demonstrated impact. Furthermore, rehabilitation trials have tended to start several months after the AMI, missing what may be a crucial period for rehabilitation. Finally, most studies have included heterogeneous groups of patients but rehabilitation may have the greatest potential in the period immediately after AMI for patients with anxiety and depression.
Sample size	7	How sample size was determined and, when applicable, explanation of any interim analyses and stopping rules.	A total of 888 patients with AMI met initial eligibility criteria and were fully screened while still in hospital. Of these, 345 were not eligible, 342 either declined randomization or were not permitted to be randomised, and 201 patients were randomised, 99 to rehabilitation and 102 to conventional community care.
Randomization -- Sequence generation	8	Method used to generate the random allocation sequence, including details of any restrictions (*e.g.*, blocking, stratification)	Random allocation to either treatment or control.
Randomization -- Allocation concealment	9	Method used to implement the random allocation sequence (*e.g.*, numbered containers or central telephone), clarifying whether the sequence was concealed until interventions were assigned.	---
Randomization -- Implementation	10	Who generated the allocation sequence, who enrolled participants, and who assigned participants to their	Allocation, sequence and enrolment were performed by the authors involved in the present investigation.

		groups.	
Blinding (masking)	11	Whether or not participants, those administering the interventions, and those assessing the outcomes were blinded to group assignment. If done, how the success of blinding was evaluated.	No information regarding blinding was mentioned.
Statistical methods	12	Statistical methods used to compare groups for primary outcome(s); Methods for additional analyses, such as subgroup analyses and adjusted analyses.	Dichotomous outcomes were analyzed using Fisher's exact test. Confidence intervals (95%) were calculated around differences in proportions. Continuous data were analyzed with a repeated measures analysis of covariance, using the baseline score as a covariate and examining effects of time and treatment and their interaction. Confidence intervals around the difference between treatments on scores at final follow-up were calculated; adjustments were made for baseline differences in the calculation of confidence intervals. In the presentation of mean differences between groups, and of confidence intervals around those differences, a negative value favors the conventional care group and a positive value favors the rehabilitation group. In each of the analyses, patients with missing data were excluded from the analysis. Additional secondary analyses included an analysis of the treatment effect at the end of the 8week intervention and an analysis that separated the most and least depressed and anxious patients (divided at the median levels), and looked at these subpopulations separately to assess the interaction between treatment and level of anxiety and depression. For purposes of analysis, patients were classified as compliant if they attended 275% of the exercise and counseling classes. The statistical significance of treatment impact on return to work was assessed with a survival analysis. This analysis used a Cox regression mode in which the variables considered were age, sex, previous AMI, site of the AMI, peak creatine phosphokinase, and blue or white collar. Because both peak creatine phosphokinase and site of the AM1 had some missing observations, the model was rerun to provide an estimate of the treatment effect, adjusting only for

			age, sex and previous AMI. Kaplan-Meier product limit estimates were used for estimating the proportion of patients in each group who ultimately returned to work.
RESULTS Participant flow	13	Flow of participants through each stage (a diagram is strongly recommended). Specifically, for each group report the numbers of participants randomly assigned, receiving intended treatment, completing the study protocol, and analyzed for the primary outcome. Describe protocol deviations from study as planned, together with reasons.	No flowchart was available
Recruitment	14	Dates defining the periods of recruitment and follow-up.	This article doesn't show the enrolment periods.
Baseline data	15	Baseline demographic and clinical characteristics of each group.	All baseline characteristics are presented on table II
Numbers analyzed	16	Number of participants (denominator) in each group included in each analysis and whether the analysis was by "intention-to-treat". State the results in absolute numbers when feasible (*e.g.*, 10/20, not 50%).	The results of the recruiting process, including reasons why those eligible were not randomised, are summarized in Table I
Outcomes and estimation	17	For each primary and secondary outcome, a summary of results for each group, and the estimated effect size and its precision (*e.g.*, 95% confidence interval).	Significantly greater improvement was seen in rehabilitation group patients at 8 weeks in the emotions dimension of a new disease-specific, health-related Quality of Life Questionnaire, in their state of anxiety and in exercise tolerance. All measures of health-related quality of life in both groups improved significantly over the 12-month follow up period.
Ancillary analyses	18	Address multiplicity by reporting any other analyses performed, including subgroup analyses and adjusted analyses, indicating those pre-specified and those exploratory.	---
Adverse events	19	All important adverse events or side effects in each intervention group.	No adverse effects were mentioned
DISCUSSION Interpretation	20	Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision and the dangers associated with multiplicity of analyses and outcomes.	Rather, the case should be made on the basis of assisting patients in regaining a productive and active life for themselves as soon as possible, as well as reducing cardiovascular risk factors, including smoking, hypertension, hypercholesterolemia and physical inactivity thus increasing the likelihood of survival after AMI.

Generalizability	21	Generalizability (external validity) of the trial findings.	Rehabilitation after AMI is aimed at speeding up the patient's return to an active and productive life.
Overall evidence	22	General interpretation of the results in the context of current evidence.	In this trial of the effects of an 8 week exercise and counseling intervention after AMI, both disease-specific and generic measures of health-related quality of life were used as the primary outcome measure. The case for cardiac rehabilitation services after AMI, individualized for appropriately selected patients, with adequate compliance over an extended period of time, should not be based solely on improved quality of life, increased exercise tolerance or return to work.

Ornish et al. (1990)

PAPER SECTION **And topic**	**Item**	**Descriptor**	**Reported on Page #**
TITLE & ABSTRACT	1	How participants were allocated to interventions (*e.g.*, "random allocation", "randomised", or "randomly assigned").	Patients were assigned to an experimental group or a usual-care control group.
INTRODUCTION Background	2	Scientific background and explanation of rationale.	The Lifestyle Heart Trial was the first randomised controlled clinical trial to determine whether patients outside hospital can be motivated to make and sustain comprehensive lifestyle changes and, if so, whether regression of coronary atherosclerosis can occur as a result of lifestyle changes alone.
METHODS Participants	3	Eligibility criteria for participants and the settings and locations where the data were collected.	Patients with angiographically documented coronary artery disease were recruited from Pacific Presbyterian Medical Centre and from Moffitt Hospital of the UCSF School of Medicine.
Interventions	4	Precise details of the interventions intended for each group and how and when they were actually administered.	Patients were individually prescribed exercise levels (typically walking) according to their baseline treadmill test results. Patients were asked to reach a target training heart rate of 50-80% of the heart rate at which 1mm ST depression occurred during baseline treadmill testing or if not ischemic to 50-80% of their age-adjusted maximum heart rate based on level of conditioning. Patients were also trained to identify exertional levels by means of the Borg rate of perceived exertion scale. Patients were asked to exercise for a minimum of 3hours per week and to spend a minimum of 30min per session exercising within their target heart rates.
Objectives	5	Specific objectives and hypotheses.	Whether lifestyle changes could affect coronary atherosclerosis after 1 year
Outcomes	6	Clearly defined primary and secondary outcome measures and, when applicable, any methods used to enhance the quality of measurements (*e.g.*, multiple observations, training of assessors).	Comprehensive lifestyle changes may be able to bring about regression or even severe coronary atherosclerosis after only 1 year without use of lipid-lowering drugs.
Sample size	7	How sample size was determined and, when applicable, explanation of any interim analyses and	A total of 193 patients who met the first five entry criteria underwent quantitative coronary arteriography.94 of these

		stopping rules.	patients met the remaining entry criteria (53 were randomly assigned to the experim.group and 43 to the control group)
Randomization -- Sequence generation	8	Method used to generate the random allocation sequence, including details of any restrictions (*e.g.*, blocking, stratification)	No information regarding randomisation were mentioned
Randomization -- Allocation concealment	9	Method used to implement the random allocation sequence (*e.g.*, numbered containers or central telephone), clarifying whether the sequence was concealed until interventions were assigned.	---
Randomization -- Implementation	10	Who generated the allocation sequence, who enrolled participants, and who assigned participants to their groups.	Allocation, sequence and enrolment were performed by the authors involved in the present investigation.
Blinding (masking)	11	Whether or not participants, those administering the interventions, and those assessing the outcomes were blinded to group assignment. If done, how the success of blinding was evaluated.	No information regarding blinding was mentioned.
Statistical methods	12	Statistical methods used to compare groups for primary outcome(s); Methods for additional analyses, such as subgroup analyses and adjusted analyses.	Differences in baseline characteristics of the two groups were tested for statistical significance by conventional t tests. Comparisons of the two study groups' baseline coronary artery lesions characteristics and changes in lesions characteristics after intervention were examined by a mixed-model analysis of variance. These analyses used lesion-specific data but allowed for the possibility that lesion data in a given subject could be statistically dependent. Mean changes in other endpoint measures were analysed for statistical significance by repeated-measures ANOVA.
RESULTS Participant flow	13	Flow of participants through each stage (a diagram is strongly recommended). Specifically, for each group report the numbers of participants randomly assigned, receiving intended treatment, completing the study protocol, and analyzed for the primary outcome. Describe protocol deviations from study as planned, together with reasons.	No flow chart was available
Recruitment	14	Dates defining the periods of recruitment and follow-up.	No recruitment or enrolment periods were mentioned.
Baseline data	15	Baseline demographic and clinical characteristics of	All data were presented in table 1.

		each group.	
Numbers analyzed	16	Number of participants (denominator) in each group included in each analysis and whether the analysis was by "intention-to-treat". State the results in absolute numbers when feasible (*e.g.*, 10/20, not 50%).	53 were randomly assigned to the experimental group and 43 to the control group.
Outcomes and estimation	17	For each primary and secondary outcome, a summary of results for each group, and the estimated effect size and its precision (*e.g.*, 95% confidence interval).	The average percentage diameter stenosis regressed from 40.0 to 37.8 in the experimental group yet progressed from 42.7 to 46.1 in the control group.
Ancillary analyses	18	Address multiplicity by reporting any other analyses performed, including subgroup analyses and adjusted analyses, indicating those pre-specified and those exploratory.	---
Adverse events	19	All important adverse events or side effects in each intervention group.	No adverse events or side effects were mentioned
DISCUSSION Interpretation	20	Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision and the dangers associated with multiplicity of analyses and outcomes.	A heterogeneous group of patients with coronary heart disease can be motivated to make comprehensive lifestyle changes for at least a year outside the hospital settings.
Generalizability	21	Generalizability (external validity) of the trial findings.	The strong relation between programme adherence and lesion changes showed that most patients needed to follow the lifestyle programme to show regression. Some important questions remain unanswered. The point of this study was to determine what is true and not what is practicable.
Overall evidence	22	General interpretation of the results in the context of current evidence.	The changes in serum lipid levels are similar to those seen with cholesterol-lowering drugs. The lifestyle intervention seems safe and compatible with other treatments of coronary heart disease. Comprehensive lifestyle changes may being to reverse coronary atherosclerosis in only a year.

Speecchia et al. (1996)

PAPER SECTION **And topic**	**Item**	**Descriptor**	**Reported on Page #**
TITLE & ABSTRACT	1	How participants were allocated to interventions (*e.g.*, "random allocation", "randomised", or "randomly assigned").	Patients with uneventful clinical courses after a first myocardial infarction were randomly assigned to a training group or a control group.
INTRODUCTION Background	2	Scientific background and explanation of rationale.	Recent meta-analysis trials have shown that exercise training reduces cardiac mortality after acute myocardial infarction. However, the mechanism of this beneficial effect is still uncertain because it is not known whether cardiac rehabilitation interacts with variables predictive of survival after myocardial infarction, particularly left ventricular function, which is the most powerful prognostic indicator in such patients. This question has practical implications because it would be desirable to identify patient subsets with various degrees of myocardial dysfunction who would take advantage of or would not benefit from an exercise training program
METHODS Participants	3	Eligibility criteria for participants and the settings and locations where the data were collected.	Over a 40-month period, 450 consecutive patients <65 years of age who had not had previous myocardial infarctions were admitted to the Cardiac Care Unit because of chest pain lasting >30 minutes and because they had a diagnosis of acute myocardial infarction based on evolutionary ECG changes and serum kinase elevation.
Interventions	4	Precise details of the interventions intended for each group and how and when they were actually administered.	Patients underwent a 4-week physical training period consisting of supervised training sessions of 30 minutes of bicycle ergometer five times a week combined with callisthenics. Training intensity was graded according to 75% of maximal work capacity reached in the previous exercise test. At the end of the 4-week training period, patients were discharged with the instructions to continue the callisthenics daily and to walk for ≥30 minutes every 2 days.
Objectives	5	Specific objectives and hypotheses.	The purpose of this study was to detect possible interactions between exercise training and predictors of prognosis after a first myocardial infarction. The long-term follow-up data were analyzed to identify prognostic indicators and to assess the

			possible interaction of exercise-based cardiac rehabilitation with variables found to be predictive of survival in this population.
Outcomes	6	Clearly defined primary and secondary outcome measures and, when applicable, any methods used to enhance the quality of measurements (*e.g.*, multiple observations, training of assessors).	Patients underwent a 4-week physical training period consisting of supervised training sessions of 30 minutes of bicycle ergometer five times a week combined with callisthenics. Training intensity was graded according to 75% of maximal work capacity reached in the previous exercise test. At the end of the 4-week training period, a second symptom-limited exercise test was performed. Patients were then discharged with the instructions to continue the callisthenics daily and to walk for ≥30 minutes every 2 days.
Sample size	7	How sample size was determined and, when applicable, explanation of any interim analyses and stopping rules.	88 patients were excluded from the study: 40 patients did not survive the acute episode and 48 had a complicated in-hospital clinical course. Of these patients, 21 had early post-infarction angina requiring urgent coronary revascularization procedures, and 27 had evidence of congestive heart failure after the first 48 hours that demanded aggressive medical therapy, including digitalis and diuretics. Another 68 patients were excluded because of chronic concomitant illnesses or musculoskeletal handicaps that would have prevented them from finishing the exercise training period. Of the remaining 294 patients, 38 did not consent to enter the study. The remaining 256 patients were included in the study.
Randomization -- Sequence generation	8	Method used to generate the random allocation sequence, including details of any restrictions (*e.g.*, blocking, stratification)	No info regarding randomisation was mentioned
Randomization -- Allocation concealment	9	Method used to implement the random allocation sequence (*e.g.*, numbered containers or central telephone), clarifying whether the sequence was concealed until interventions were assigned.	---
Randomization -- Implementation	10	Who generated the allocation sequence, who enrolled participants, and who assigned participants to their groups.	Allocation, sequence and enrolment were performed by the authors involved in the present investigation.
Blinding (masking)	11	Whether or not participants, those administering the	No information regarding blinding was mentioned.

		interventions, and those assessing the outcomes were blinded to group assignment. If done, how the success of blinding was evaluated.	
Statistical methods	12	Statistical methods used to compare groups for primary outcome(s); Methods for additional analyses, such as subgroup analyses and adjusted analyses.	Student's *t* test was used to compare mean values, and a χ^2 test was used to compare the incidence of discrete variables between the two groups. Univariate analysis was carried out by the Kaplan-Meier method, and significance was tested by the log-rank test. A total of 86 variables were considered. Multivariate analysis was performed by use of the Cox regression model for censored survival data. Interactions between exercise training and prognostic indicators also were searched for to assess whether the impact of treatment in a given patient would depend in some way on the value of one or more prognostic indicators. Kaplan-Meier analysis revealed that five variables were significantly related to cumulative probability of cardiac death: persistence of ST-segment elevation in the ECG leads showing abnormal Q waves, cardiomegaly on radiographic examination, an exercise duration <9 minutes, a blood pressure increase of <30 mm Hg during exercise testing and ejection fraction.
RESULTS Participant flow	13	Flow of participants through each stage (a diagram is strongly recommended). Specifically, for each group report the numbers of participants randomly assigned, receiving intended treatment, completing the study protocol, and analyzed for the primary outcome. Describe protocol deviations from study as planned, together with reasons.	No flow chart was available.
Recruitment	14	Dates defining the periods of recruitment and follow-up.	The periods were not mentioned but it lasted 40 months.
Baseline data	15	Baseline demographic and clinical characteristics of each group.	All baseline data are presented on table 1.
Numbers analyzed	16	Number of participants (denominator) in each group included in each analysis and whether the analysis was by "intention-to-treat". State the results in absolute numbers when feasible (*e.g.*, 10/20, not 50%).	The 256 patients were randomised either to a 4-week training period (125 patients) or a control group (131 patients). Medical treatment consisted of í-blockers in 17 group 1 patients and 13 group 2 patients, nitrates or calcium antagonists in 107 group 1 patients and 113 group 2 patients,

			and low doses of diuretics in 11 group 1 patients and 13 group 2 patients. No patient was taking digitalis. After a mean follow-up period of 34.5 months, 18 patients (5 in group 1 and 13 in group 2) had cardiac deaths (14 had sudden deaths; 4 had fatal myocardial infarctions). Eighteen patients underwent bypass surgery (11 patients in group 1 and 7 in group 2). Patients were operated on because of chest pain that was unresponsive to medical treatment (15 patients) or because of a significant left main disease (3 patients) after a mean time period of 8.4 months (range, 1 to 38 months) from randomization
Outcomes and estimation	17	For each primary and secondary outcome, a summary of results for each group, and the estimated effect size and its precision (*e.g.*, 95% confidence interval).	Patients with a first myocardial infarction represent the majority of all patients with acute infarction (60% to 80%).Although these patients have less mechanical dysfunction than patients without previous infarctions, the most potent prognostic variables are those relating to the extent of myocardial damage after the infarction
Ancillary analyses	18	Address multiplicity by reporting any other analyses performed, including subgroup analyses and adjusted analyses, indicating those pre-specified and those exploratory.	---
Adverse events	19	All important adverse events or side effects in each intervention group.	No patients died because of operation or in the subsequent follow-up period. Two patients (1 in group 1 and 1 in group 2) underwent successful coronary angioplasty. To avoid any potential effect of these revascularization procedures on survival, these patients were excluded from survival analysis at the time of bypass surgery or coronary angioplasty.
DISCUSSION Interpretation	20	Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision and the dangers associated with multiplicity of analyses and outcomes.	The effects of exercise-based cardiac rehabilitation on mortality after myocardial infarction remain unclear because difficulties in study design (lack of randomization and control groups, inadequate study group size) have precluded definite conclusions
Generalizability	21	Generalizability (external validity) of the trial findings.	The change in the autonomic balance induced by physical training may be beneficial in other ways besides preventing life-threatening arrhythmias in high-risk patients. Elevated

			sympathetic activity, by increasing the wall stress and loading condition of the myocardium, further deteriorates cardiac function by worsening the process of ventricular remodelling. Training-induced increases in parasympathetic activity may limit the deleterious effects of sympathetic hyperactivity on left ventricular performance, particularly in patients with low ejection fractions.
Overall evidence	22	General interpretation of the results in the context of current evidence.	Exercise training could exert a beneficial effect by inducing a change in the autonomic balance of the heart. Strong evidence links the autonomic nervous system to cardiovascular mortality after myocardial infarction. Myocardial ischemia and infarction can impair autonomic innervation to and from the heart, thus modulating the development of cardiac arrhythmias.

Stähle et al. (1999)

PAPER SECTION **And topic**	**Item**	**Descriptor**	**Reported on Page #**
TITLE & ABSTRACT	1	How participants were allocated to interventions (*e.g.*, "random allocation", "randomised", or "randomly assigned").	Patients were randomised to either a supervised out patients group-training programme or to a control group.
INTRODUCTION Background	2	Scientific background and explanation of rationale.	In the early years of exercise rehabilitation of patients with coronary heart disease, an age exceeding 65 years was on arbitrary grounds a frequently used exclusion criterion. A limitation with this and other similar studies is that they compared the elderly with younger patients or with normal subjects in the same age-cohort. Thus there are no properly designed trials that have specifically addressed the efficacy and safety of exercise training in an elderly population with coronary artery disease.
METHODS Participants	3	Eligibility criteria for participants and the settings and locations where the data were collected.	Consecutive patients aged 65 years and up who were admitted to the Coronary Care Unit at the Karolinska Hospital Stockholm because of an acute coronary event were eligible. All patients gave their informed consent to participate. The study was approved by the Local Ethics Committee.
Interventions	4	Precise details of the interventions intended for each group and how and when they were actually administered.	The patients participated in a 50 min aerobic outpatient group-training programme (including warm-up and cool-down) three times a week for 3 months. The training was followed by 10 min of music-supported relaxation.
Objectives	5	Specific objectives and hypotheses.	This study evaluated the physiological effects and self-reported quality of life after an aerobic outpatient group-training programme in subjects above the age of 65 years.
Outcomes	6	Clearly defined primary and secondary outcome measures and, when applicable, any methods used to enhance the quality of measurements (*e.g.*, multiple observations, training of assessors).	---
Sample size	7	How sample size was determined and, when applicable, explanation of any interim analyses and stopping rules.	56 patients were randomised to group 1 and 53 to group C.

Randomization -- Sequence generation	8	Method used to generate the random allocation sequence, including details of any restrictions (*e.g.*, blocking, stratification)	No more information regarding randomisation was mentioned.
Randomization -- Allocation concealment	9	Method used to implement the random allocation sequence (*e.g.*, numbered containers or central telephone), clarifying whether the sequence was concealed until interventions were assigned.	---
Randomization -- Implementation	10	Who generated the allocation sequence, who enrolled participants, and who assigned participants to their groups.	Allocation, sequence and enrolment were performed by the authors involved in the present investigation.
Blinding (masking)	11	Whether or not participants, those administering the interventions, and those assessing the outcomes were blinded to group assignment. If done, how the success of blinding was evaluated.	No information regarding blinding was mentioned.
Statistical methods	12	Statistical methods used to compare groups for primary outcome(s); Methods for additional analyses, such as subgroup analyses and adjusted analyses.	Results were presented as mean, standard deviation and range or median and range. Analyses were performed using a two-way ANOVA with repeated measurers on one factor, and two-sided Student's paired and unpaired t-tests. All variables were tested with ANOVA for changes over time within and between the 2 groups. Differences at baseline were explored by Student's test. Analyses were also performed using the Mann-Whitney U-test for the comparison between the treatment groups concerning the effect of intervention after 3 and 12 months. Statistically significant differences were assumed when $p<0.05$
RESULTS Participant flow	13	Flow of participants through each stage (a diagram is strongly recommended). Specifically, for each group report the numbers of participants randomly assigned, receiving intended treatment, completing the study protocol, and analyzed for the primary outcome. Describe protocol deviations from study as planned, together with reasons.	No flow chart was available.
Recruitment	14	Dates defining the periods of recruitment and follow-up.	The recruitment was conducted during the period October 1994 to June 1997.
Baseline data	15	Baseline demographic and clinical characteristics of each group.	All baseline characteristics were mentioned in table 1.

Numbers analyzed	16	Number of participants (denominator) in each group included in each analysis and whether the analysis was by "intention-to-treat". State the results in absolute numbers when feasible (*e.g.*, 10/20, not 50%).	8 patients were withdrawn because of coronary artery bypass surgery, lack of time participating in the training program, moved from the area or for orthopaedic reasons. In all, 101 patients completed the follow-up.
Outcomes and estimation	17	For each primary and secondary outcome, a summary of results for each group, and the estimated effect size and its precision (*e.g.*, 95% confidence interval).	The compliance in the training group was 87%. Exercise tolerance increased in the trained group from 104 to 122 and 111 W after 3 and 12 months respectively. The corresponding values were 102, 105 and 105 W among controls. Parameters, such as quality of life, self-estimated level of physical activity, fitness and well-being were graded higher by the trained patients than those who served as controls of the two occasions of follow-up.
Ancillary analyses	18	Address multiplicity by reporting any other analyses performed, including subgroup analyses and adjusted analyses, indicating those pre-specified and those exploratory.	---
Adverse events	19	All important adverse events or side effects in each intervention group.	No adverse effects were mentioned.
DISCUSSION Interpretation	20	Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision and the dangers associated with multiplicity of analyses and outcomes.	Many patients in the large and increasing group of elderly subjects recovering from acute coronary events are eligible for active rehabilitation. An aerobic group training programme seems to be an efficient tool to improve their physical fitness and feeling of well-being.
Generalizability	21	Generalizability (external validity) of the trial findings.	Physical training cannot be completely separated from more multifactorial rehabilitative and preventive interventions. All patients had access to a professional team specialized in cardiac rehabilitation, including medical follow-up at the outpatient clinic.
Overall evidence	22	General interpretation of the results in the context of current evidence.	Although both groups improved, the overall improvement in quality of life variables was substantially more marked in the intervention group. This may, at least partly, be related to the opportunity for the trained patients to repeatedly stress themselves under professional supervision. Exercise-based programmes have been

			shown not to only affect physical exercise capacity. They also have implication on every day life by positively affecting the musculoskeletal system, improving osteoporosis, joint flexibility, muscle strength and endurance as well as balance.

Taylor (1997)

PAPER SECTION **And topic**	**Item**	**Descriptor**	**Reported on Page #**
TITLE & ABSTRACT	1	How participants were allocated to interventions (*e.g.*, "random allocation", "randomised", or "randomly assigned").	Patients were randomised to a control group, a group who only attended education/information sessions and a group who additionally participated in an exercise programme.
INTRODUCTION Background	2	Scientific background and explanation of rationale.	Whilst 74% of health districts in the UK provide cardiac rehabilitation, the programmes are generally not been subjected to formal assessment and the objectives are often unclear. There is also a lack of consensus concerning optimal rehabilitation programmes for specific patients groups with wide variations.
METHODS Participants	3	Eligibility criteria for participants and the settings and locations where the data were collected.	54 patients of either sex recovering from their 1st MI were assigned between the 3 study groups.
Interventions	4	Precise details of the interventions intended for each group and how and when they were actually administered.	A six-week rehabilitation programme was designed, which comprised of weekly discussion and information sessions and an individually prescribed aerobic training programme. The discussion sessions were led by a multidisciplinary team comprising a nurse, physiotherapist and occupational therapist. A dietician and a medical social worker were also involved in some of the sessions. The six areas of focus for the discussions were: resumption of functional activity, recognition and management of stress, management of coronary heart disease, medication, and healthy eating. The 30-min training programme consisted predominantly of cycling on a static bicycle preceded by 5-10 min of step-ups and was performed at the hospital three times a week. Patients exercised at heart rates equivalent to 40-50% measured peak oxygen uptake. This intensity was determined from treadmill exercise tolerance tests performed prior to entering the programme. Low-intensity programmes have been shown to evoke similar changes to those observed with high intensity training

			and enhance compliance. During the exercise training sessions, the heart rate was monitored at intervals by the radial pulse and the patients were shown how to perform this in order to monitor themselves when performing the exercise regime at home on non-attendance days. The intensity of the exercises was progressively increased from 40% peak oxygen uptake to 50% during the six weeks to accommodate improvements in fitness. The progression was based upon the heart rate during the exercise sessions and the patient's rate of perceived exertion.
Objectives	5	Specific objectives and hypotheses.	The objectives of this study were to determine whether patients derived psychosocial benefits form an early cardiac rehabilitation programme following an uncomplicated MI and whether the benefits were influenced by the type of programme offered.
Outcomes	6	Clearly defined primary and secondary outcome measures and, when applicable, any methods used to enhance the quality of measurements (*e.g.*, multiple observations, training of assessors).	---
Sample size	7	How sample size was determined and, when applicable, explanation of any interim analyses and stopping rules.	No significant differences were found between the groups for any clinical features. The control group were given 'routine care' comprising informal advice and British Heart Foundation literature; the education group only attended the discussion/information sessions of the rehabilitation programme and the exercise group attended both the discussion/information sessions and participated in a supervised exercise training programme. Patients were recruited between four and five days after their infarction and enrolled into the study within ten days post MI.
Randomization -- Sequence generation	8	Method used to generate the random allocation sequence, including details of any restrictions (*e.g.*, blocking, stratification)	No information regarding randomisation was mentioned.
Randomization --	9	Method used to implement the random allocation sequence	---

Allocation concealment		(*e.g.*, numbered containers or central telephone), clarifying whether the sequence was concealed until interventions were assigned.	
Randomization -- Implementation	10	Who generated the allocation sequence, who enrolled participants, and who assigned participants to their groups.	Allocation, sequence and enrolment were performed by the authors involved in the present investigation.
Blinding (masking)	11	Whether or not participants, those administering the interventions, and those assessing the outcomes were blinded to group assignment. If done, how the success of blinding was evaluated.	No information regarding blinding was mentioned.
Statistical methods	12	Statistical methods used to compare groups for primary outcome(s); Methods for additional analyses, such as subgroup analyses and adjusted analyses.	All measurements were performed upon entry into the study between seven and ten days after infarction and repeated at the end of the intervention period (week 6) and three months later (week 18, approximately five months post MI). The change from entry to the end of the six-week programme and completion of the study was determined for each patient and used in a Kruskal Wallis one-way analysis of variance to identify differences between the three groups. A level of P 0.05 or less was considered significant. Summary measures are presented as medians with 95% confidence intervals.
RESULTS Participant flow	13	Flow of participants through each stage (a diagram is strongly recommended). Specifically, for each group report the numbers of participants randomly assigned, receiving intended treatment, completing the study protocol, and analyzed for the primary outcome. Describe protocol deviations from study as planned, together with reasons.	No flow chart was available
Recruitment	14	Dates defining the periods of recruitment and follow-up.	No enrolment periods were mentioned.
Baseline data	15	Baseline demographic and clinical characteristics of each group.	All data were presented in table 1.
Numbers analyzed	16	Number of participants (denominator) in each group included in each analysis and whether the analysis was by "intention-to-treat". State the results in absolute numbers when feasible (*e.g.*, 10/20, not 50%).	All 54 patients who entered the study completed the six-week intervention period. 5 were withdrawn during the 12-week follow-up period due to changes in drug management. This affected 2patients in the control and exercise groups and 1 in the education only group. The

			patients showed wide variations in results, which is clearly shown by the large 95% confidence interval accompanying the median for each group.
Outcomes and estimation	17	For each primary and secondary outcome, a summary of results for each group, and the estimated effect size and its precision (*e.g.*, 95% confidence interval).	The patients who attended the six week exercise and education programme showed significantly greater improvements in anxiety, rehabilitation status and walking activity compared to the other 2groups. Those who only attended the education sessions did not show any significant over the control group.
Ancillary analyses	18	Address multiplicity by reporting any other analyses performed, including subgroup analyses and adjusted analyses, indicating those pre-specified and those exploratory.	---
Adverse events	19	All important adverse events or side effects in each intervention group.	No adverse events occurred during the period of supervised exercise or exercise tests.
DISCUSSION Interpretation	20	Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision and the dangers associated with multiplicity of analyses and outcomes.	Patients in the early stages of recovery after an uncomplicated MI derived psychosocial benefits when the rehabilitation programme includes an individual, supervised exercise regime. Patients recovering from an uncomplicated MI did not appear to derive any benefit from only attending an education-based programme.
Generalizability	21	Generalizability (external validity) of the trial findings.	Exercise training has a marked effect on the functional status of the patients with AMI. All patients experienced a large increase in the proportion of the time they were active and for most patients this increase was attributable to longer periods of activity at all levels of intensity. This increase in activity is important not only for its influence on the patient's quality of life but also for its possible effect on the pathophysiology of the condition.
Overall evidence	22	General interpretation of the results in the context of current evidence.	Those recovering from an uncomplicated MI derived psychosocial benefits from participating in an exercise training program. Their improvements cannot be attributed entirely to the exercise programme, but may represent the additive effects of the two components.

Tsoukas, Andonakoudis & Christakos (1995)

PAPER SECTION **And topic**	**Item**	**Descriptor**	**Reported on Page #**
TITLE & ABSTRACT	1	How participants were allocated to interventions (*e.g.*, "random allocation", "randomised", or "randomly assigned").	Patients either underwent modest level exercise training for 3 months or did not participate in this program.
INTRODUCTION Background	2	Scientific background and explanation of rationale.	Exercise training is used widely in the rehabilitation of patients with coronary artery disease as an established method. The well-documented benefits of training include increased maximal functional capacity and decreased heart rate and systolic blood pressure response to submaximal workload.
METHODS Participants	3	Eligibility criteria for participants and the settings and locations where the data were collected.	The patient's population consisted of 113 patients with uncomplicated myocardial infarction documented by chest pain, evolving electrocardiogram changes and increases in plasma enzyme levels.
Interventions	4	Precise details of the interventions intended for each group and how and when they were actually administered.	Exercise training was performed on ergometric bicycle, 4 times weekly with equal intermediate intervals for 3 months. Each session included 5 periods of 5 minutes of exercise on a bicycle with 2minute rest intervals.
Objectives	5	Specific objectives and hypotheses.	This study was undertaken to determine whether adaptations to short-term exercise training after myocardial infarction, could affect the response of heart rate, blood pressure and double product at submaximal workload and the behaviour of electrocardiographic ST segment depression.
Outcomes	6	Clearly defined primary and secondary outcome measures and, when applicable, any methods used to enhance the quality of measurements (*e.g.*, multiple observations, training of assessors).	---
Sample size	7	How sample size was determined and, when applicable,	Patients underwent clinical examination, ECG,

		explanation of any interim analyses and stopping rules.	echocardiogram, 24-hour Holter monitoring and symptom-limited bicycle exercise test of low intensity
Randomization -- Sequence generation	8	Method used to generate the random allocation sequence, including details of any restrictions (*e.g.*, blocking, stratification)	No information regarding randomisation was mentioned.
Randomization -- Allocation concealment	9	Method used to implement the random allocation sequence (*e.g.*, numbered containers or central telephone), clarifying whether the sequence was concealed until interventions were assigned.	---
Randomization -- Implementation	10	Who generated the allocation sequence, who enrolled participants, and who assigned participants to their groups.	Allocation, sequence and enrolment were performed by the authors involved in the present investigation.
Blinding (masking)	11	Whether or not participants, those administering the interventions, and those assessing the outcomes were blinded to group assignment. If done, how the success of blinding was evaluated.	No information regarding blinding was mentioned.
Statistical methods	12	Statistical methods used to compare groups for primary outcome(s); Methods for additional analyses, such as subgroup analyses and adjusted analyses.	Data were expressed as mean values. Comparison between groups of patients was performed by using unpaired t test.
RESULTS Participant flow	13	Flow of participants through each stage (a diagram is strongly recommended). Specifically, for each group report the numbers of participants randomly assigned, receiving intended treatment, completing the study protocol, and analyzed for the primary outcome. Describe protocol deviations from study as planned, together with reasons.	No flow chart was available.
Recruitment	14	Dates defining the periods of recruitment and follow-up.	No enrolment periods were mentioned
Baseline data	15	Baseline demographic and clinical characteristics of each group.	No data were presented.
Numbers analyzed	16	Number of participants (denominator) in each group included in each analysis and whether the analysis was by "intention-to-treat". State the results in absolute numbers when feasible (*e.g.*, 10/20, not 50%).	52 patients attended all 48 exercise sessions.
Outcomes and estimation	17	For each primary and secondary outcome, a summary of results for each group, and the estimated effect size and its	There was no significant difference in heart rate, systolic blood pressure and double product at

		precision (*e.g.*, 95% confidence interval).	rest before the treadmill stress between the two groups.
Ancillary analyses	18	Address multiplicity by reporting any other analyses performed, including subgroup analyses and adjusted analyses, indicating those pre-specified and those exploratory.	---
Adverse events	19	All important adverse events or side effects in each intervention group.	No adverse effects were mentioned.
DISCUSSION Interpretation	20	Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision and the dangers associated with multiplicity of analyses and outcomes.	Cardiac rehabilitation with supervised exercise training has been shown to be a useful component of comprehensive management of patients with different forms of coronary artery disease. The benefits of rehabilitation include in-creased physical activity, less psychological disability, better management in secondary prevention of ischemic heart disease, lower incidence of recurrent infarction, improvement of survival in coronary patients and increase in the incidence of patients who return to work after an acute myocardial infarction.
Generalizability	21	Generalizability (external validity) of the trial findings.	With the achievement by exercise training of lower heart rate and double product at submaximal exercise, the myocardial oxygen consumption required to achieve a workload is decreased. The mechanisms through which this benefit is produced have been extensively investigated and include improved efficiency of peripheral musculature by increasing mitochondrial mass and oxygen extraction and decreased circulating catecholamines at submaximal workloads. There is no evidence of improvement in myocardial collateral circulation. Likewise, improved left ventricular function, as evaluated with such parameters as resting ejection fraction, has not consistently improved

			in patients with coronary artery disease, although there is possible improvement in exertional ejection fraction especially after long-term exercise training.
Overall evidence	22	General interpretation of the results in the context of current evidence.	In patients who suffered a recent acute uncomplicated myocardial infarction, a 3-month period of modest bicycle exercise training with increasing intensity was sufficient to induce a favourable decrease in the heart rate, systolic blood pressure, and double product at submaximal workload levels (3d and 5th minute of treadmill stress test according to Bruce protocol). The exercise tolerance was increased in patients who participated in the cardiac rehabilitation program as they succeeded better exercise time in the treadmill stress test.

Vona et al. (2004)

PAPER SECTION **And topic**	**Item**	**Descriptor**	**Reported on Page #**
TITLE & ABSTRACT	1	How participants were allocated to interventions (*e.g.*, "random allocation", "randomised", or "randomly assigned").	Patients were randomised to either a training group or a control group
INTRODUCTION Background	2	Scientific background and explanation of rationale.	There is evidence that aerobic exercise improves endothelial function in healthy subjects as well as in patients with chronic heart failure. However, it is unknown whether this effect occurs in patients with recent myocardial infarction (AMI).
METHODS Participants	3	Eligibility criteria for participants and the settings and locations where the data were collected.	All consecutive male and female patients, aged 70 years and more, who were referred to a cardiac rehabilitation program after a first uncomplicated AMI The protocol was approved by the local Ethical Committee. Written informed consent was obtained from all patients before randomization.
Interventions	4	Precise details of the interventions intended for each group and how and when they were actually administered.	The patients of the training group underwent moderate aerobic training 3 times a week. Each session included a 10-minute warm-up, 40 minutes of cycling on a cycle ergometer with telemetry monitoring and intensity set at 75% of peak exercise heart rate as measured in the second ECG stress testing, and a 10-minute cool-down. Patients were also encouraged to increase their daily physical activity level on the nontraining days by walking more, climbing stairs, and so forth.
Objectives	5	Specific objectives and hypotheses.	The objectives of the present study were (1) to quantify endothelial dysfunction in patients with recent uncomplicated AMI; (2) to determine the effects of a moderate exercise

			training program on brachial artery vasomotor reactivity in patients not receiving pharmacologic therapy with statins and/or ACE inhibitors; and (3) to evaluate the effects of detraining 1 month after the completion of regular training.
Outcomes	6	Clearly defined primary and secondary outcome measures and, when applicable, any methods used to enhance the quality of measurements (*e.g.*, multiple observations, training of assessors).	Vascular endothelium plays a major role in the modulation of vascular tone and in cardiovascular homeostasis. Endothelial dysfunction, in particular impaired endothelium-dependent vasodilation is associated with early atherosclerosis.
Sample size	7	How sample size was determined and, when applicable, explanation of any interim analyses and stopping rules.	Inclusion criteria were: ability to exercise absence of previous cardiovascular events, absence of major modifiable coronary risk factors (i.e., normal total and low-density lipoprotein [LDL] cholesterol, no diabetes, no hypertension, non smoker or ex-smoker, left ventricular ejection fraction <45%, and echocardiographic absence of ventricular hypertrophy. Patients taking calcium antagonists, statins, or ACE inhibitors, patients with hemodynamically significant valvular heart disease, cardiopulmonary bypass surgery, chronic lung disease, systemic and/or hematologic illness were excluded
Randomization -- Sequence generation	8	Method used to generate the random allocation sequence, including details of any restrictions (*e.g.*, blocking, stratification)	No information regarding randomisation was mentioned.
Randomization -- Allocation concealment	9	Method used to implement the random allocation sequence (*e.g.*, numbered containers or central telephone), clarifying whether the sequence was concealed until interventions were assigned.	---
Randomization -- Implementation	10	Who generated the allocation sequence, who enrolled participants, and who assigned participants to their groups.	Allocation, sequence and enrolment were performed by the authors involved in the present investigation.

Blinding (masking)	11	Whether or not participants, those administering the interventions, and those assessing the outcomes were blinded to group assignment. If done, how the success of blinding was evaluated.	No information regarding blinding was mentioned.
Statistical methods	12	Statistical methods used to compare groups for primary outcome(s); Methods for additional analyses, such as subgroup analyses and adjusted analyses.	Once the images for analysis had been chosen, the boundaries for diameter measurements were identified manually with electronic callipers. Measurements were taken from the centre of the "m" line of the anterior wall to the centre of the posterior wall in telediastole, incident with the R wave on a continuously recorded electrocardiogram. Each observer analyzed 5 cardiac cycles for each scan and the measurements were averaged. Measurements were performed at baseline, during FMD, and after the CP and NTG tests. Changes in vessel diameter were calculated for each subject as the percentage variation of the arterial diameter under different stimuli compared to the baseline diameter.
RESULTS Participant flow	13	Flow of participants through each stage (a diagram is strongly recommended). Specifically, for each group report the numbers of participants randomly assigned, receiving intended treatment, completing the study protocol, and analyzed for the primary outcome. Describe protocol deviations from study as planned, together with reasons.	No flow diagram was available.
Recruitment	14	Dates defining the periods of recruitment and follow-up.	Between February, 2001 and February, 2002
Baseline data	15	Baseline demographic and clinical characteristics of each group.	All baseline demographic data were presented in table 1.
Numbers analyzed	16	Number of participants (denominator) in each group included in each analysis and whether the analysis was by "intention-to-treat". State the results in absolute numbers when feasible (*e.g.*, 10/20, not 50%).	Of the 968 patients referred for the rehabilitation program, 54 (5.6%) met the inclusion criteria. All the patients underwent coronary angiography immediately after hospitalization, and 35% of them underwent coronary angioplasty with stent positioning during or immediately after the acute

			phase of myocardial infarction. All the patients were being treated with b-blockers and aspirin at the time of investigation.
Outcomes and estimation	17	For each primary and secondary outcome, a summary of results for each group, and the estimated effect size and its precision (*e.g.*, 95% confidence interval).	No significant differences were found between G1 and G2 patients regarding age, gender, site and dimension of myocardial infarction, or left ventricular ejection fraction. In line with our inclusion criteria, the sample considered was at low cardiac risk: the majority of the patients had limited extension of coronary artery disease and only 7.1% of the G1 and 8.3% of G2 patients had angiographically demonstrated 3-vessel disease. Total cholesterol was slightly but significantly higher in G, while the other metabolic parameters considered (LDL and HDL cholesterol, triglycerides, and glycemia) and body mass index were not significantly different. Peak exercise heart rate, blood pressure, rate pressure product, and work rate were similar on initial ECG stress testing.
Ancillary analyses	18	Address multiplicity by reporting any other analyses performed, including subgroup analyses and adjusted analyses, indicating those pre-specified and those exploratory.	---
Adverse events	19	All important adverse events or side effects in each intervention group.	All G1 patients and 24 of the 26 G2 patients completed the follow-up. No adverse events occurred in either group during the follow-up.
DISCUSSION Interpretation	20	Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision and the dangers associated with multiplicity of analyses and outcomes.	Training-induced improvements do not appear to last in the long term. The correlation between changes in brachial artery vasodilation and changes in exercise capacity supports the hypothesis that exercise tolerance might partially depend on endothelial function.
Generalizability	21	Generalizability (external validity) of the trial findings.	Exercise increases shear stress, which is a strong physiological stimulus for NO release: the

			FMD increase after physical training has been observed in both animals and humans and the mechanism is likely to involve a chronic increase in NO production mediated by an increase in the expression of NO-synthase. NO-synthase mrNA is upregulated in cultured endothelial cells exposed to laminar shear stress, and similar observations have been reported in animal studies involving both short-and long-term exercise
Overall evidence	22	General interpretation of the results in the context of current evidence.	The major contributions of the present study are the following: (1) brachial vasoreactivity appears to be severely impaired 3 weeks after an uncomplicated AMI; (2) training significantly contributes to systemic improvement of this endothelial dysfunction, reducing the response to sympathetic stimuli such as the CP test; (3) changes in endothelial function are associated with changes in exercise tolerance; (4) the effects disappear after 1 month of detraining. These findings indicate that regular aerobic training is an effective lifestyle intervention for reversing the loss of endothelium-dependent vasodilation in patients with a recent myocardial infarction, but that the exercise must be continued over time.

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PAPER SECTION **And topic**	**Item**	**Descriptor**	**Reported on Page #**
TITLE & ABSTRACT	1	How participants were allocated to interventions (*e.g.*, "random allocation", "randomised", or "randomly assigned").	Patients were randomised to either a cardiac rehabilitation and prevention group or a conventional therapy group.
INTRODUCTION Background	2	Scientific background and explanation of rationale.	A cardiac rehabilitation and prevention program is a recognized non-pharmacological modality in the management of coronary heart disease. However, the effect of a CRPP on systolic function of the heart is controversial, and no data exists on diastolic function in CHD.
METHODS Participants	3	Eligibility criteria for participants and the settings and locations where the data were collected.	269 consecutive patients with CHD who were enrolled into the cardiac rehabilitation centre. They had either recent AMI or elective PCI within the past 6 weeks and were randomised into either CRPP or conventional therapy. All the study subjects were regularly followed up in the cardiac rehabilitation clinic. The study protocol was approved by the Ethics Committee and informed written consent was obtained from every patient.
Interventions	4	Precise details of the interventions intended for each group and how and when they were actually administered.	Phase 1 was an inpatient ambulating program which lasted for 7 to 14 days. Phase 2 was a twice-weekly outpatient exercise and education program lasting for 8 weeks. Each session included 1 hour of education class followed by 2 hours of exercise training. The first hour of training was conducted by a physiotherapist who concentrated on aerobic cardiovascular training. It consisted of 5 minutes of stretching followed by endurance training for at least 30 minutes, which included

			treadmill, ergometer, rowing, stepping, or arm ergometer, with some resistance training for the rest of the period, including dumbbell or weight training depending on the patient's condition and exercise capacity. The intensity of the training was gradually increased in the first 3 to 4 weeks until reaching 65% to 85% of age-adjusted heart rate reserve. In patients who had low chronotropic response due to b-blocker therapy, a training effect of up to 30 beats above resting heart rate was used. The next hour of training was conducted by an occupational therapist in which domiciliary or vocational environment-focused training was performed. Phase 3 was a community-based home exercise program for another 6 months. This consisted of daily walking exercise for at least 60 minutes after warm-up exercise. The control group attended a 2-hour talk that explained the disease, the importance of risk factor modification, and potential benefits of physical activity, but did not undergo the outpatient exercise-training program.
Objectives	5	Specific objectives and hypotheses.	To examine if exercise training conducted in a structured CRPP was able to improve resting systolic and diastolic functions, and if the changes in resting cardiac function could predict the change in exercise capacity in patients with CHD who had recent AMI or had undergone elective PCI.
Outcomes	6	Clearly defined primary and secondary outcome measures and, when applicable, any methods used to enhance the quality of measurements (*e.g.*, multiple observations, training of assessors).	Early studies of studies are needed to confirm the benefit of CRPP on a cardiac rehabilitation program (CRPP) in the form of exercise capacity. Furthermore, the mechanisms of exercise training and education classes have

			shown improvement of exercise tolerance after CRPP. These mechanisms include improvements with CHD.
Sample size	7	How sample size was determined and, when applicable, explanation of any interim analyses and stopping rules.	There were 269 patients randomised, of whom 193 had a recent AMI (129 in the CRPP and 64 in the control groups) and 76 had an elective PCI (52 in the CRPP and 24 in the control groups).
Randomization -- Sequence generation	8	Method used to generate the random allocation sequence, including details of any restrictions (*e.g*., blocking, stratification)	No information regarding randomisation was mentioned
Randomization -- Allocation concealment	9	Method used to implement the random allocation sequence (*e.g*., numbered containers or central telephone), clarifying whether the sequence was concealed until interventions were assigned.	---
Randomization -- Implementation	10	Who generated the allocation sequence, who enrolled participants, and who assigned participants to their groups.	Allocation, sequence and enrolment were performed by the authors involved in the present investigation.
Blinding (masking)	11	Whether or not participants, those administering the interventions, and those assessing the outcomes were blinded to group assignment. If done, how the success of blinding was evaluated.	No information regarding blinding was mentioned.
Statistical methods	12	Statistical methods used to compare groups for primary outcome(s); Methods for additional analyses, such as subgroup analyses and adjusted analyses.	Data were analyzed using a statistical software program (SPSS for Windows, V.10.0, SPSS Inc, Chicago, Ill). The difference in mean between parametric variables in various phases was compared by paired sample t test. The difference in mean between parametric variables of CRPP and control groups was compared by unpaired t test. The comparison of categorical data between 2 or more groups was performed by Pearson 2 test. The relation between parametric variables was examined by correlation analysis. Data were expressed as mean standard deviation. A P value <.05 was

			considered as statistical significant.
RESULTS Participant flow	13	Flow of participants through each stage (a diagram is strongly recommended). Specifically, for each group report the numbers of participants randomly assigned, receiving intended treatment, completing the study protocol, and analyzed for the primary outcome. Describe protocol deviations from study as planned, together with reasons.	No flow chart was available
Recruitment	14	Dates defining the periods of recruitment and follow-up.	No enrolment periods were mentioned
Baseline data	15	Baseline demographic and clinical characteristics of each group.	All data were presented in table 1.
Numbers analyzed	16	Number of participants (denominator) in each group included in each analysis and whether the analysis was by "intention-to-treat". State the results in absolute numbers when feasible (*e.g.*, 10/20, not 50%).	There were 269 patients randomised, of whom 193 had a recent AMI (129 in the CRPP and 64 in the control groups) and 76 had an elective PCI (52 in the CRPP and 24 in the control groups).
Outcomes and estimation	17	For each primary and secondary outcome, a summary of results for each group, and the estimated effect size and its precision (*e.g.*, 95% confidence interval).	There was no change in resting and peak heart rate, resting and peak blood pressure, or peak rate-pressure product between CRPP and control groups nor when patients were stratified into AMI and PCI subgroups. Since these parameters could be affected by b-blockers, the data were further analyzed according to the status of this drug therapy. In patients using b-blocker therapy (75%), the resting systolic blood pressure was significantly lower in phase 3 in the CRPP than control group but was not different for patients not using b-blocker therapy.
Ancillary analyses	18	Address multiplicity by reporting any other analyses performed, including subgroup analyses and adjusted analyses, indicating those pre-specified and those exploratory.	---
Adverse events	19	All important adverse events or side effects in each intervention group.	Diastolic dysfunction is very common in patients with CHD, especially among those with LV contractile dysfunction. In addition, the

			progressive worsening of diastolic function may lead to gradual deterioration of cardiac function, which eventually may present as clinical heart failure. Patients whose contractile reserve is already jeopardized as the result of a previous AMI are especially vulnerable. Therefore, measures envisaged to improve diastolic performance, such as CRPP, can improve exercise capacity and might even alter the course of the disease favourably and in selected patients. This latter concept needs to be confirmed by large clinical trials with longer duration of follow up.
DISCUSSION Interpretation	20	Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision and the dangers associated with multiplicity of analyses and outcomes.	Exercise training has a neutral effect on systolic function and hence the latter did not predict the improvement of exercise time in phase 3.
Generalizability	21	Generalizability (external validity) of the trial findings.	In patients with coronary heart disease, cardiac rehabilitation and prevention group is effective in preventing the deterioration of diastolic dysfunction in both ventricles.
Overall evidence	22	General interpretation of the results in the context of current evidence.	It remains controversial whether resting systolic function is improved by exercise training and changes in resting diastolic function of the ventricles after exercise training in patients with coronary heart disease have not been studied to date, particular in those with preserved systolic function.